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(12) **United States Patent**
Py

(10) **Patent No.: US 8,240,521 B2**
(45) **Date of Patent: Aug. 14, 2012**

(54) **FLUID DISPENSER HAVING A ONE-WAY VALVE, PUMP, VARIABLE-VOLUME STORAGE CHAMBER, AND A NEEDLE PENETRABLE AND LASER RESEALABLE PORTION**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 448 days.

(21) Appl. No.: **11/351,716**

(22) Filed: **Feb. 10, 2006**

(65) **Prior Publication Data**

US 2006/0131338 A1 Jun. 22, 2006

Related U.S. Application Data

(63) Continuation of application No. 10/890,465, filed on Jul. 12, 2004, now Pat. No. 7,000,806, which is a continuation of application No. 10/001,745, filed on Oct. 23, 2001, now Pat. No. 6,761,286.

(60) Provisional application No. 60/242,595, filed on Oct. 23, 2000, provisional application No. 60/242,974, filed on Oct. 24, 2000.

(51) **Int. Cl.**
B65D 5/72 (2006.01)

(52) **U.S. Cl.** **222/492**; 222/183; 222/386.5; 222/321.2; 222/1

(58) **Field of Classification Search** 222/95, 222/105, 386.5, 402.1–402.25, 491–494, 222/1

See application file for complete search history.

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Assistant Examiner — Melvin Cartagena
(74) *Attorney, Agent, or Firm* — McCarter & English, LLP

(57) **ABSTRACT**

A dispenser for dispensing a fluid includes a rigid vial that has a main fluid chamber containing a fluid, and a pump assembly that is in fluid communication with the main fluid chamber and is configured to dispense a predetermined quantity of fluid from the main fluid chamber. A flexible bladder is provided which is located within the main fluid chamber and is configured to expand to fill the ullage created within the main fluid chamber during dispensing of fluid by the pump assembly. The resilient bladder tends to force itself outwardly toward the rigid vial and, in turn, increases the pressure within the main fluid chamber in comparison to the interior of the bladder to thereby prevent the ingress of air or vapors through the bladder or otherwise into the main fluid chamber.

20 Claims, 20 Drawing Sheets

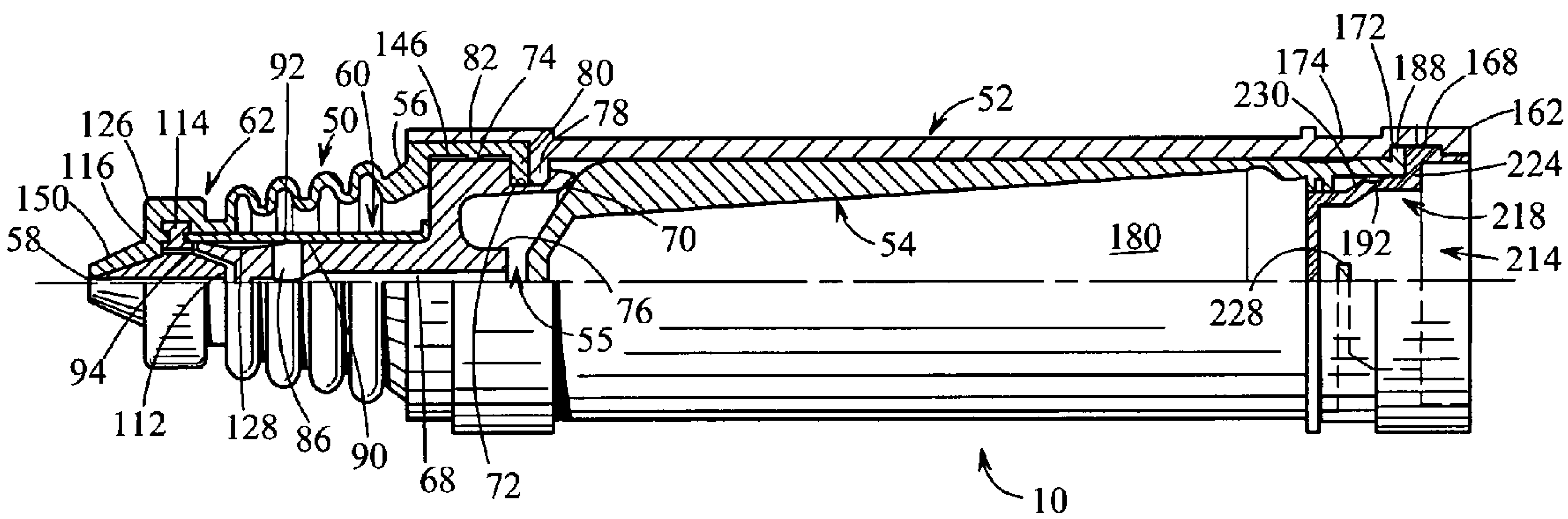

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FIG. 1

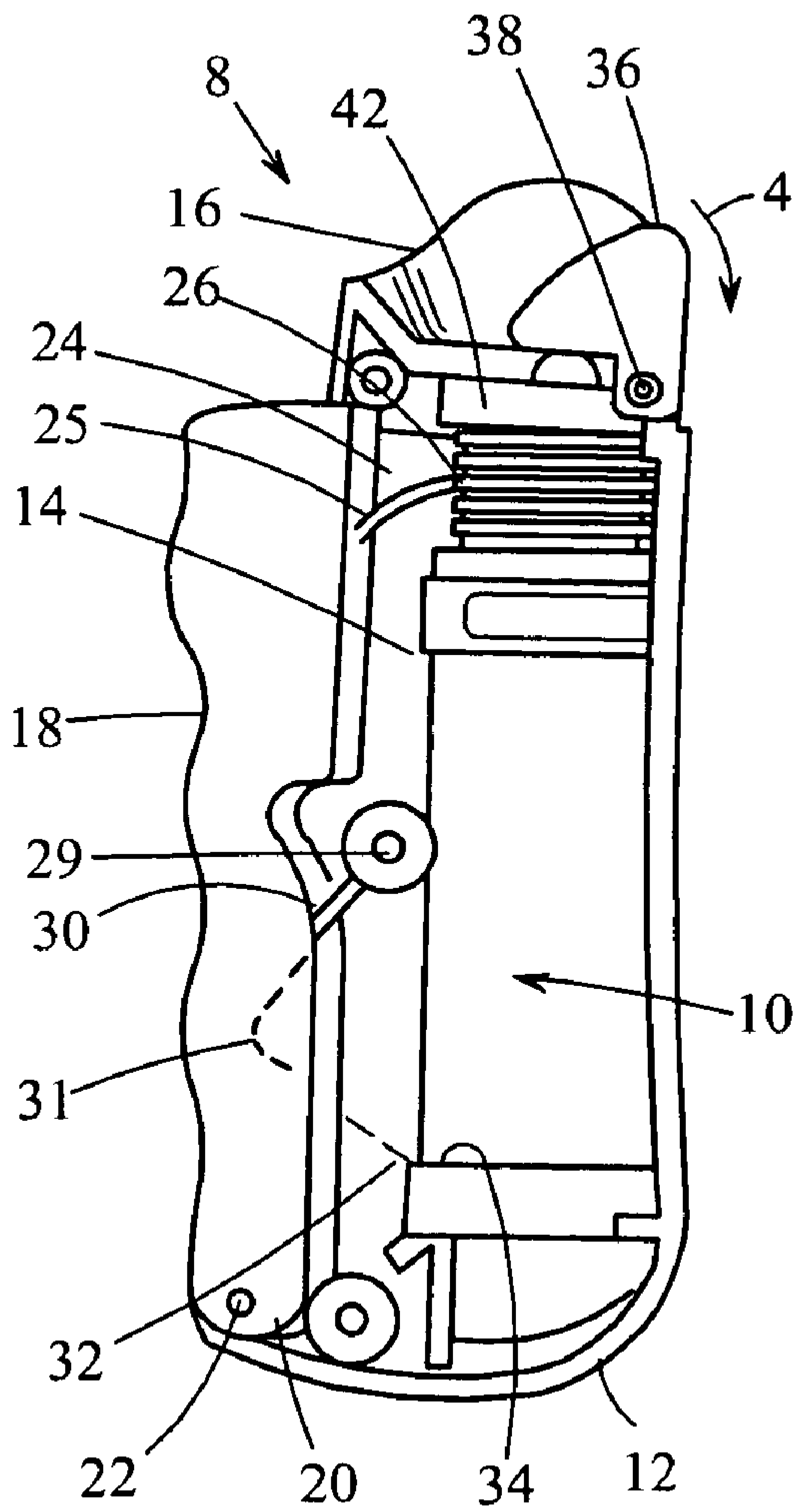
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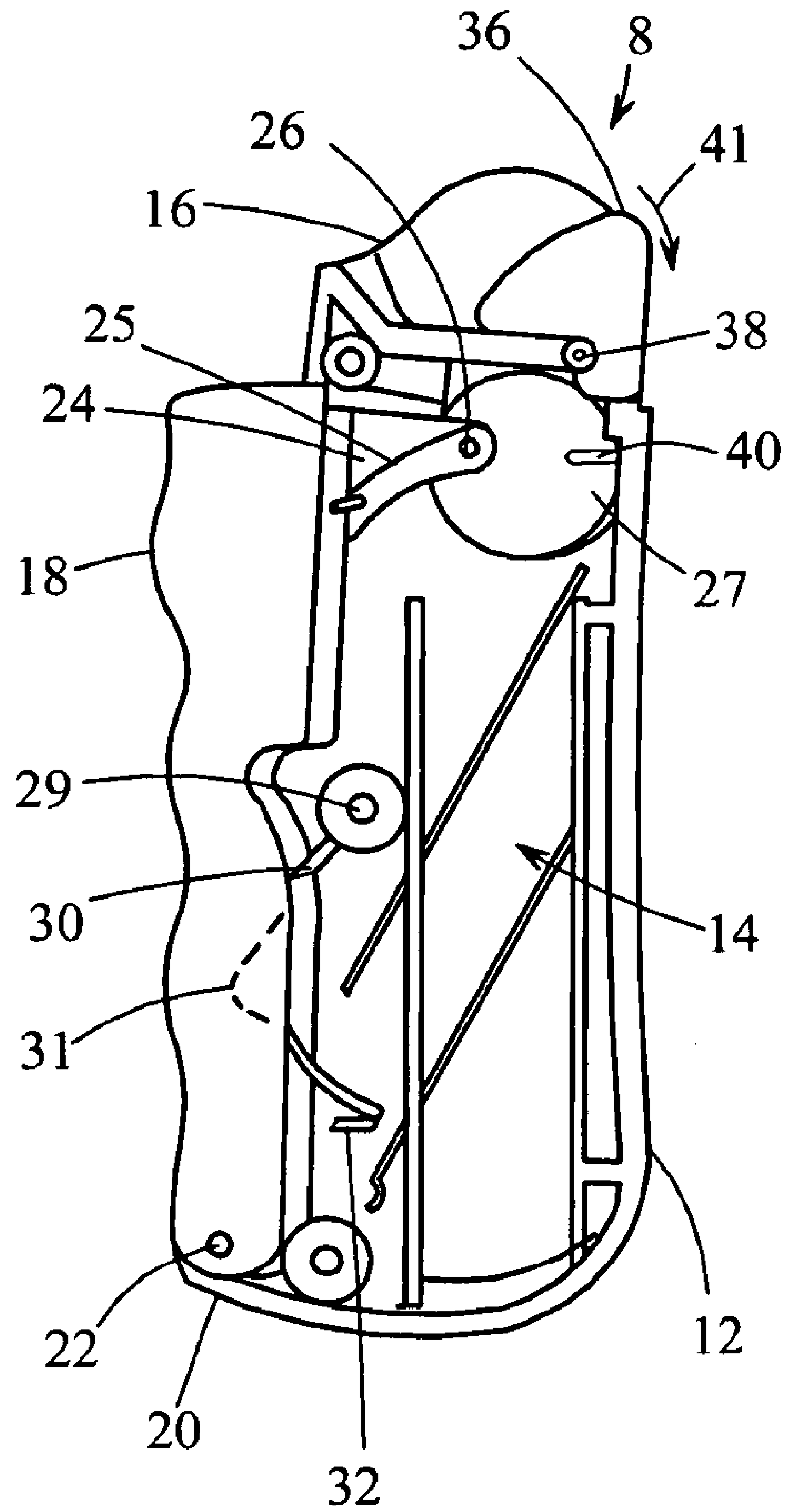
FIG. 1A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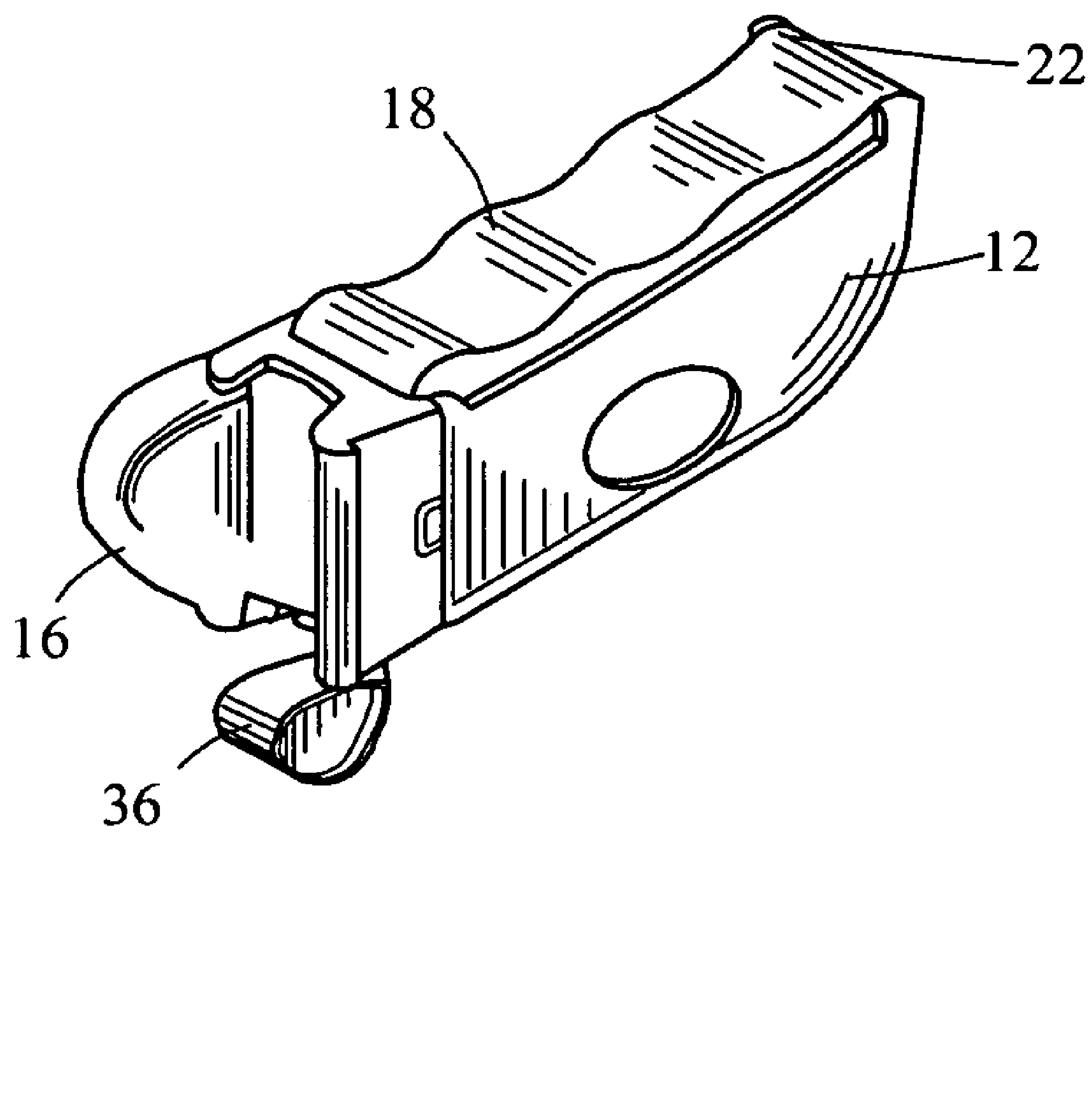

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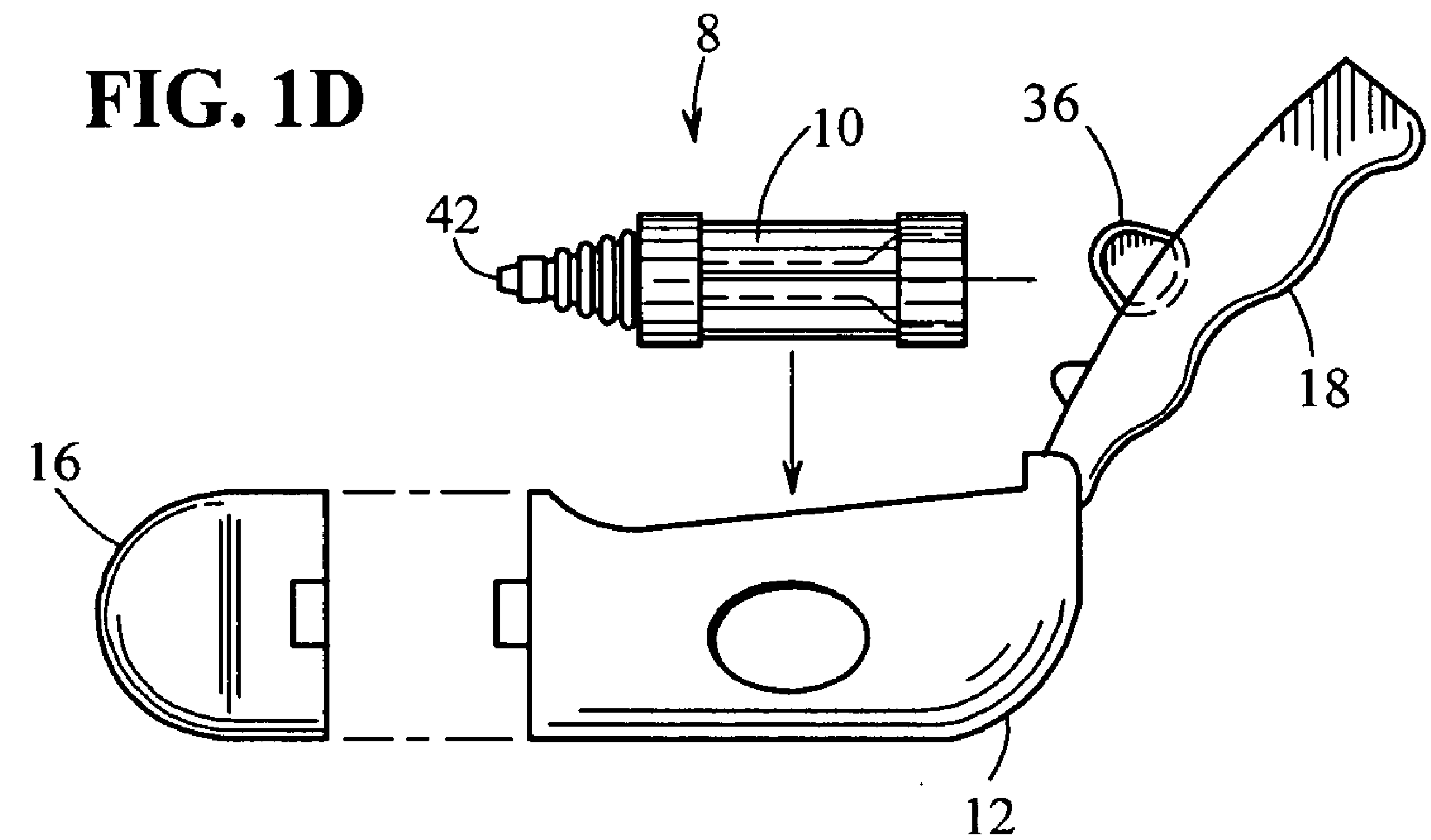

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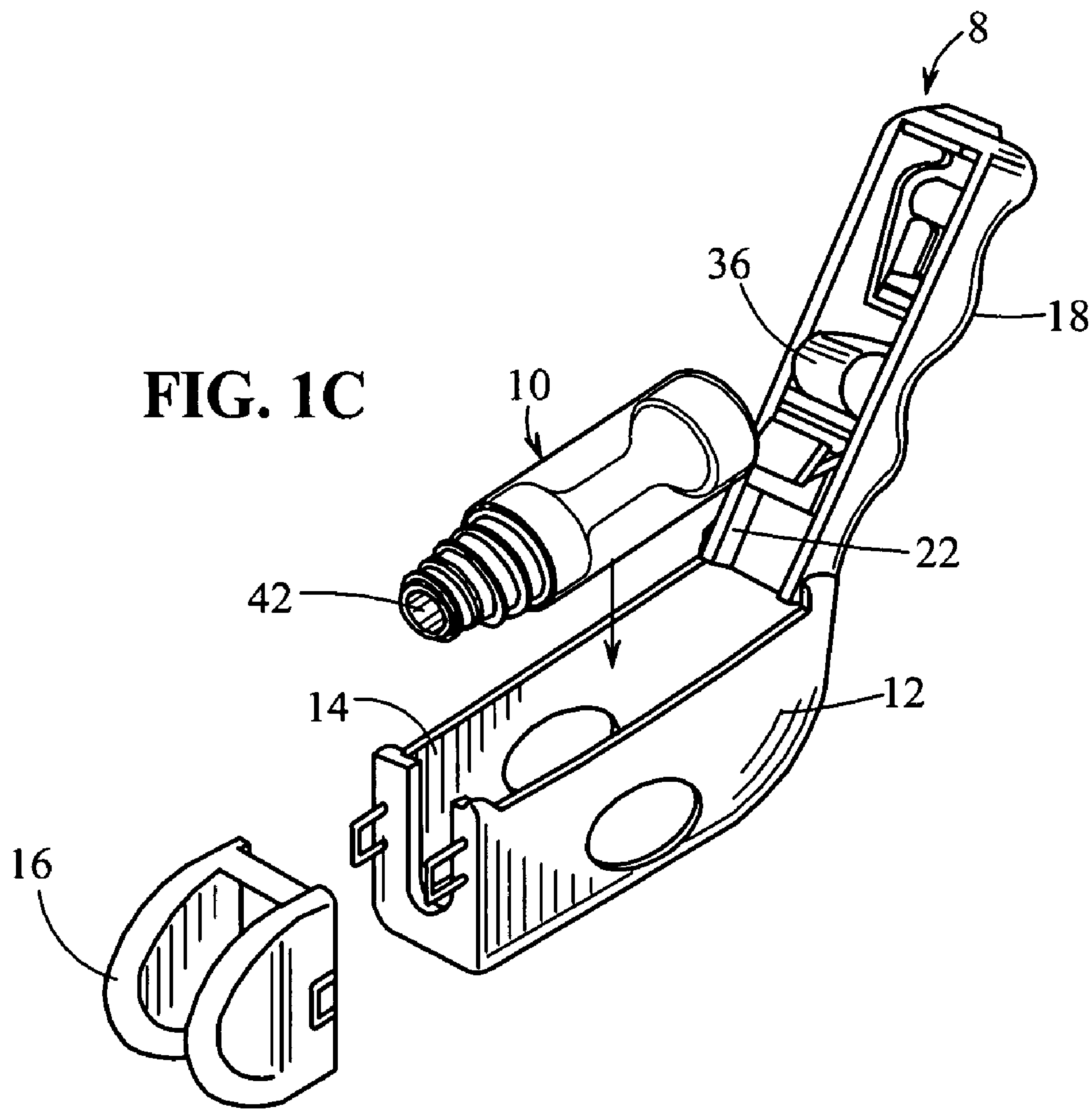

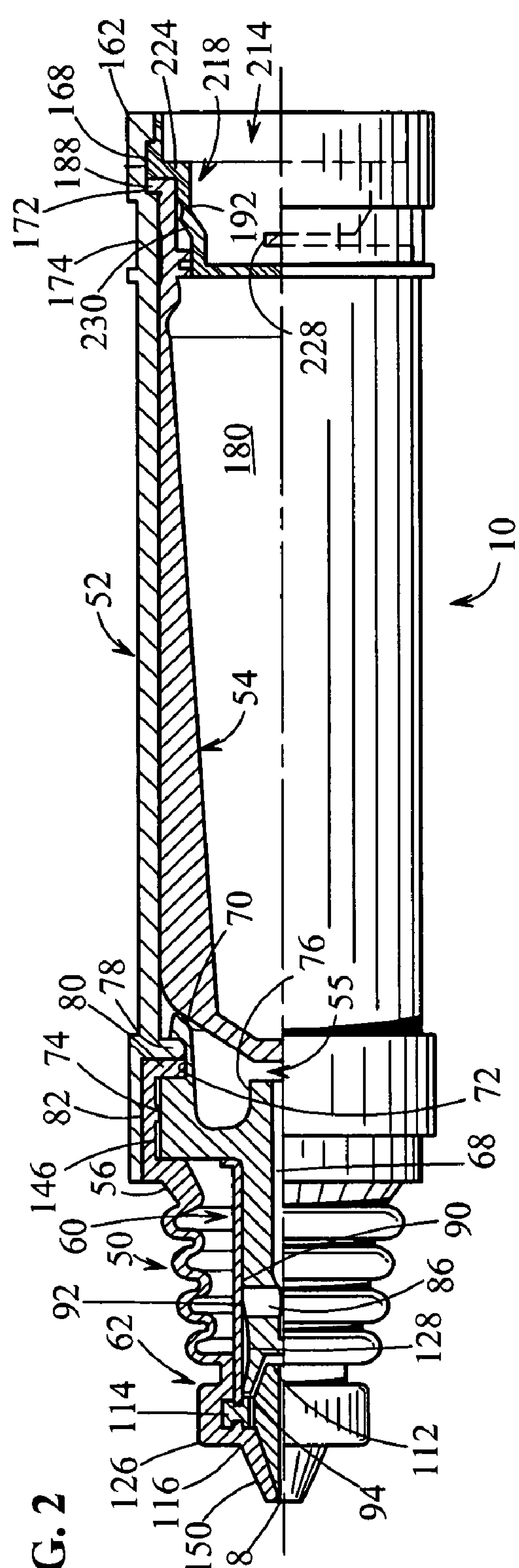

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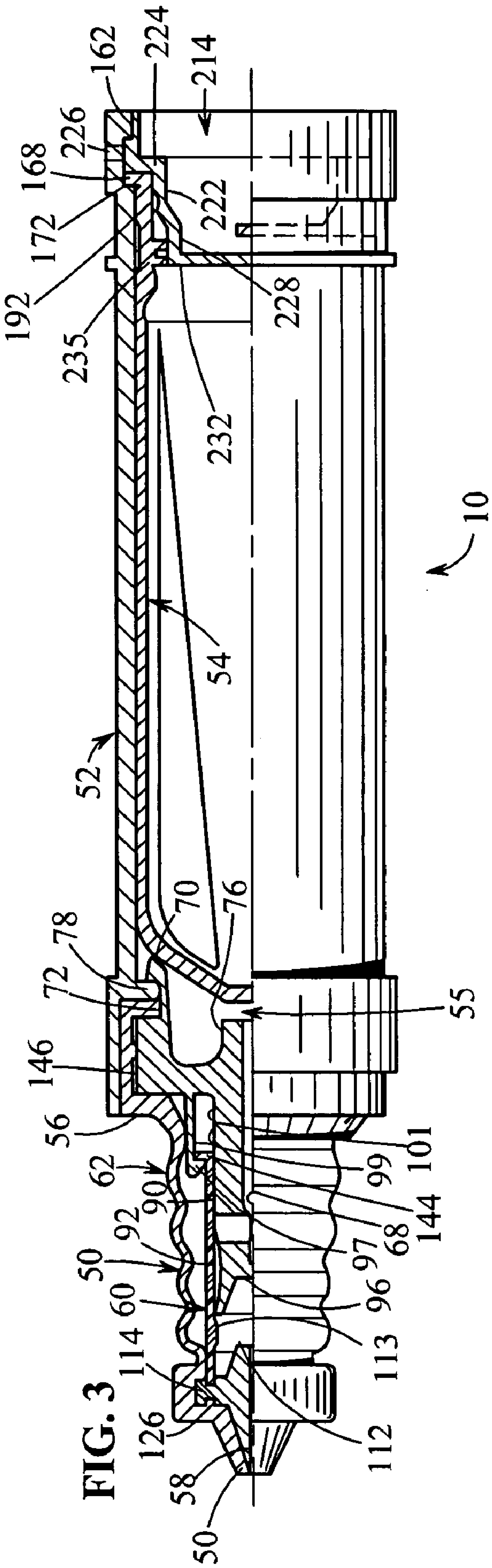
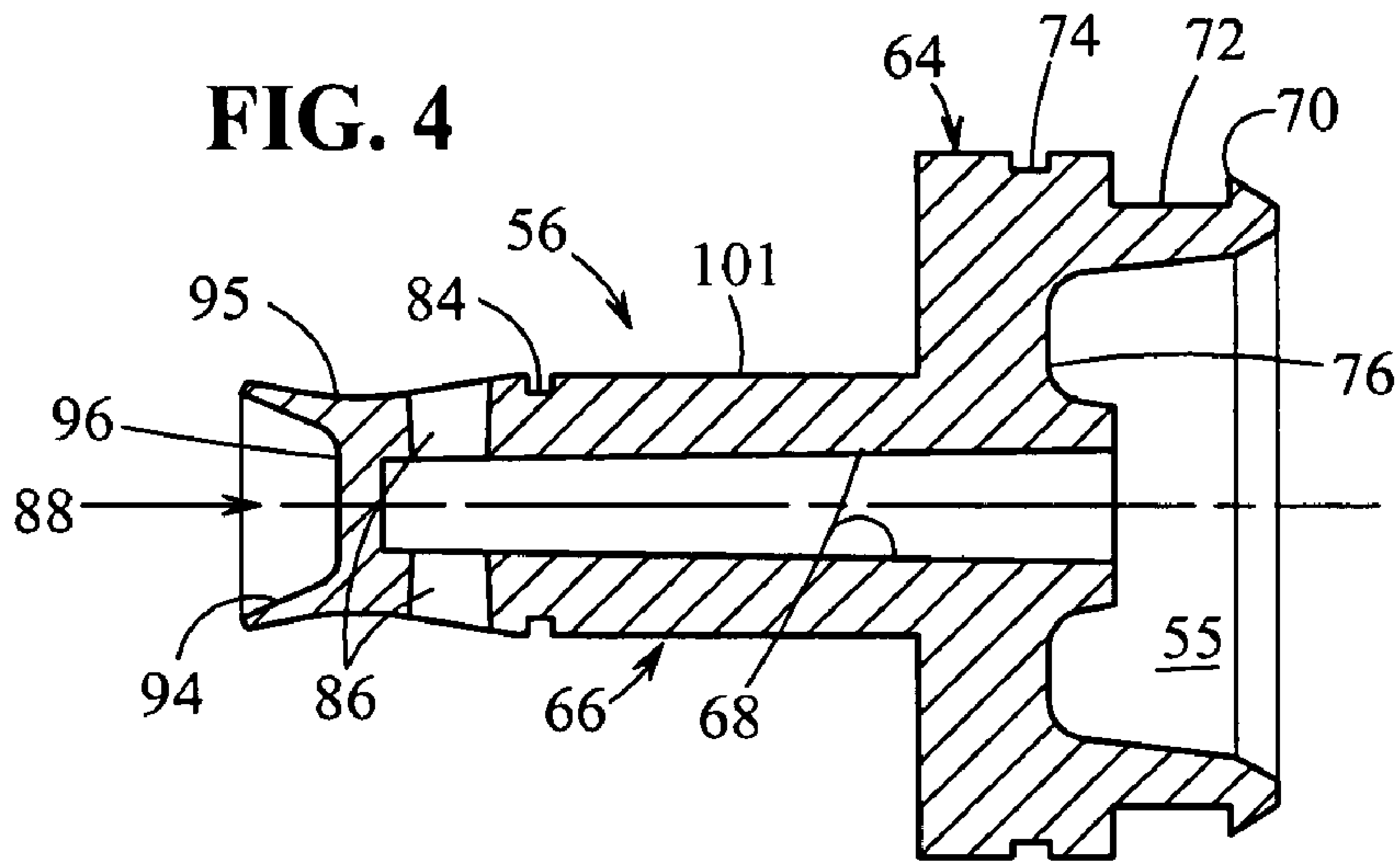


FIG. 3

FIG. 4



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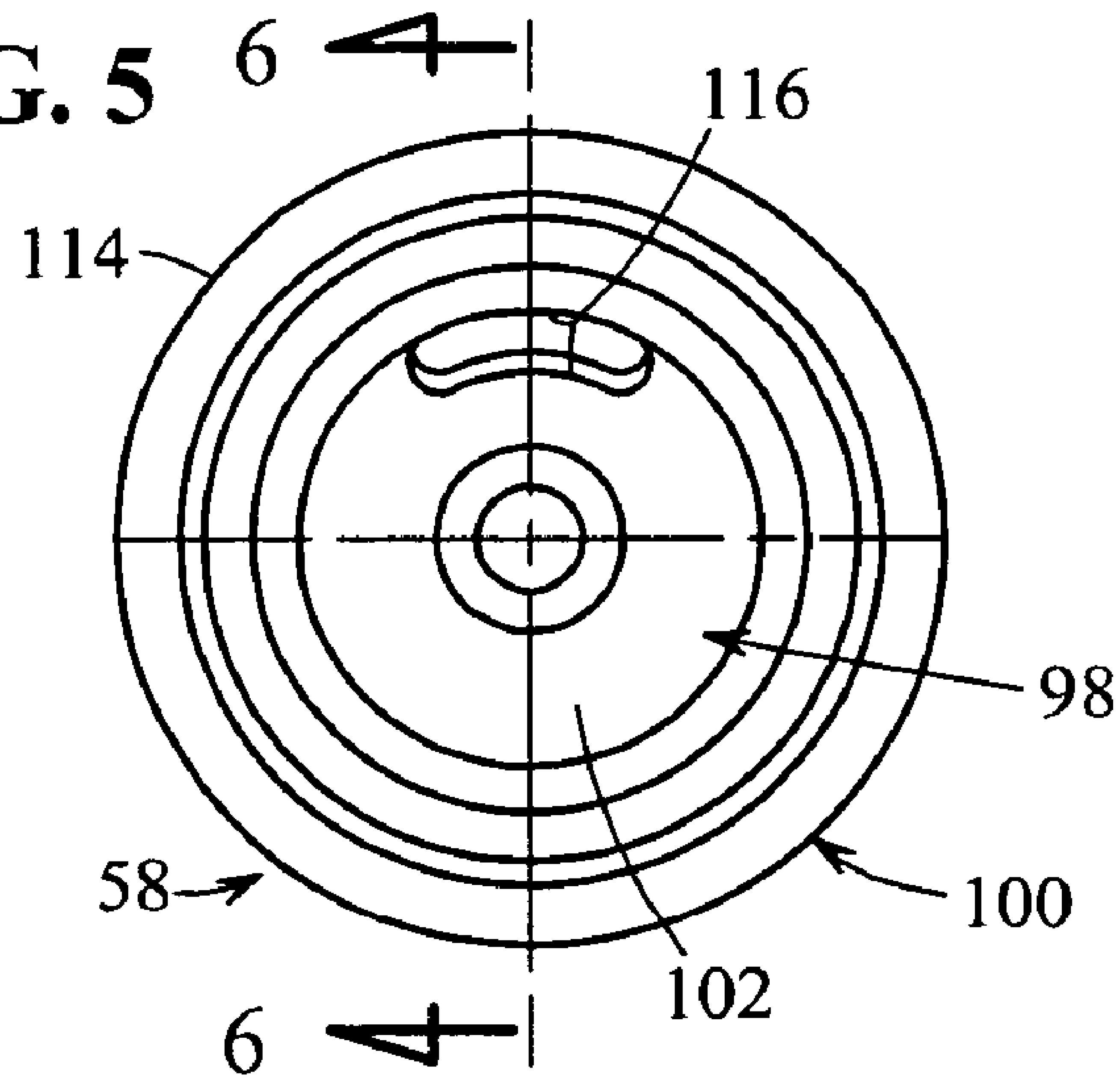

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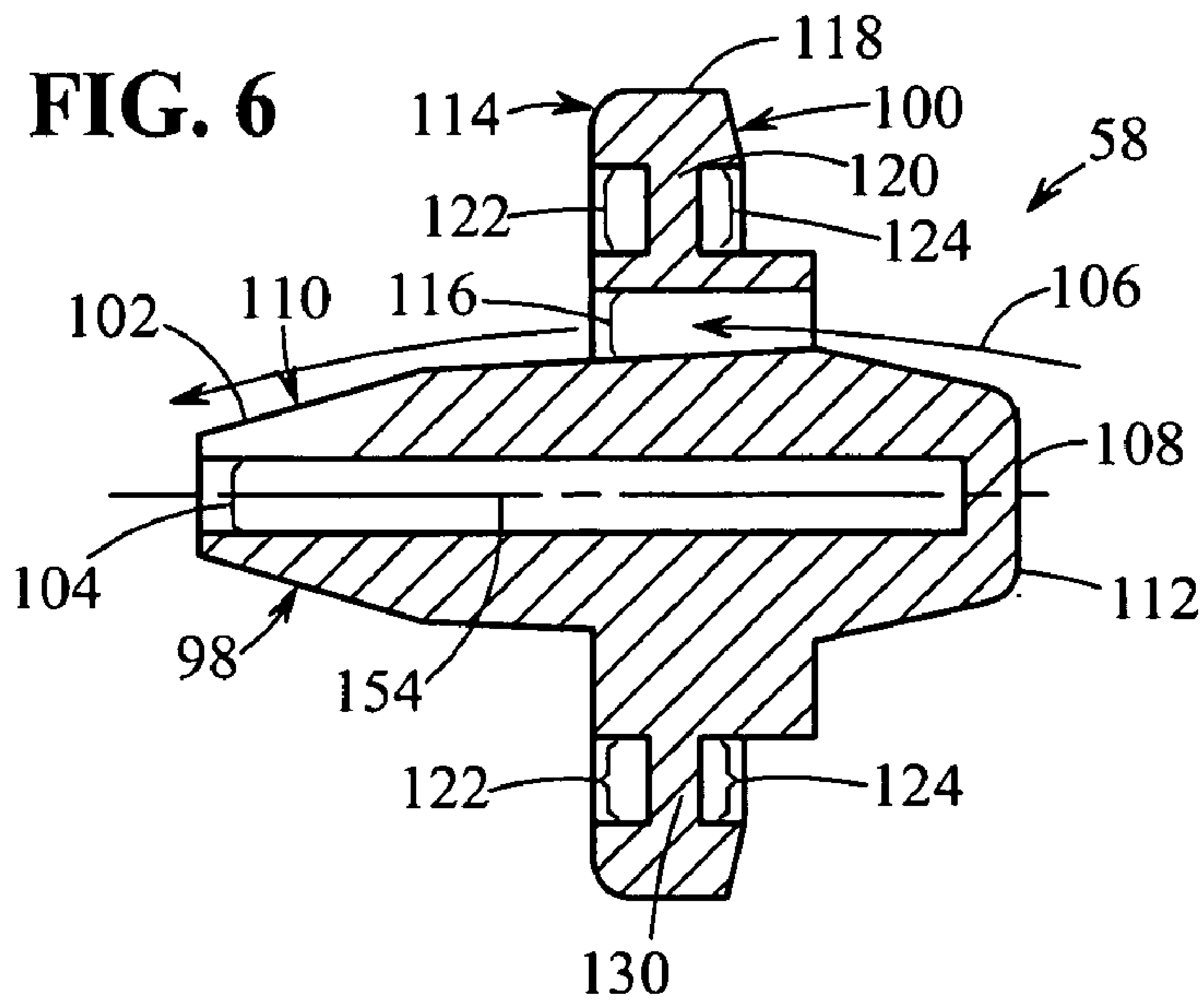

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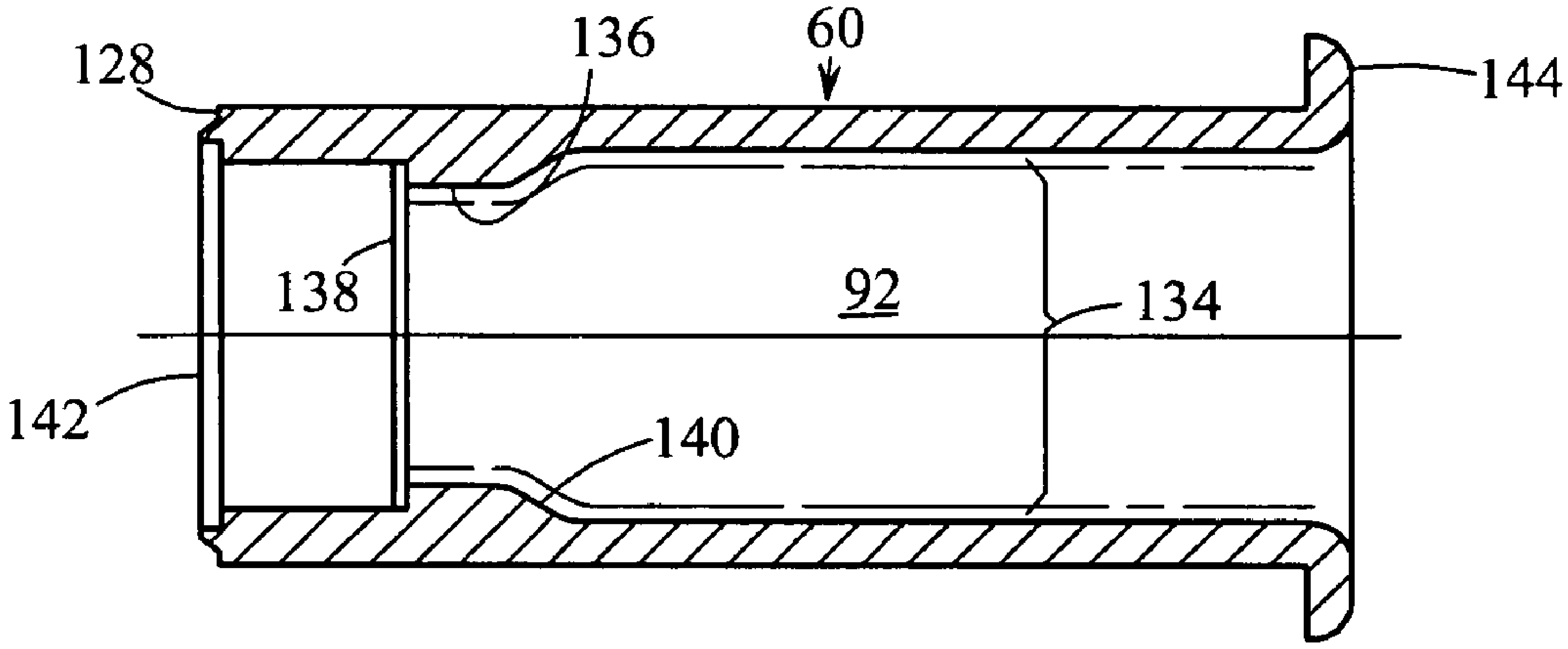

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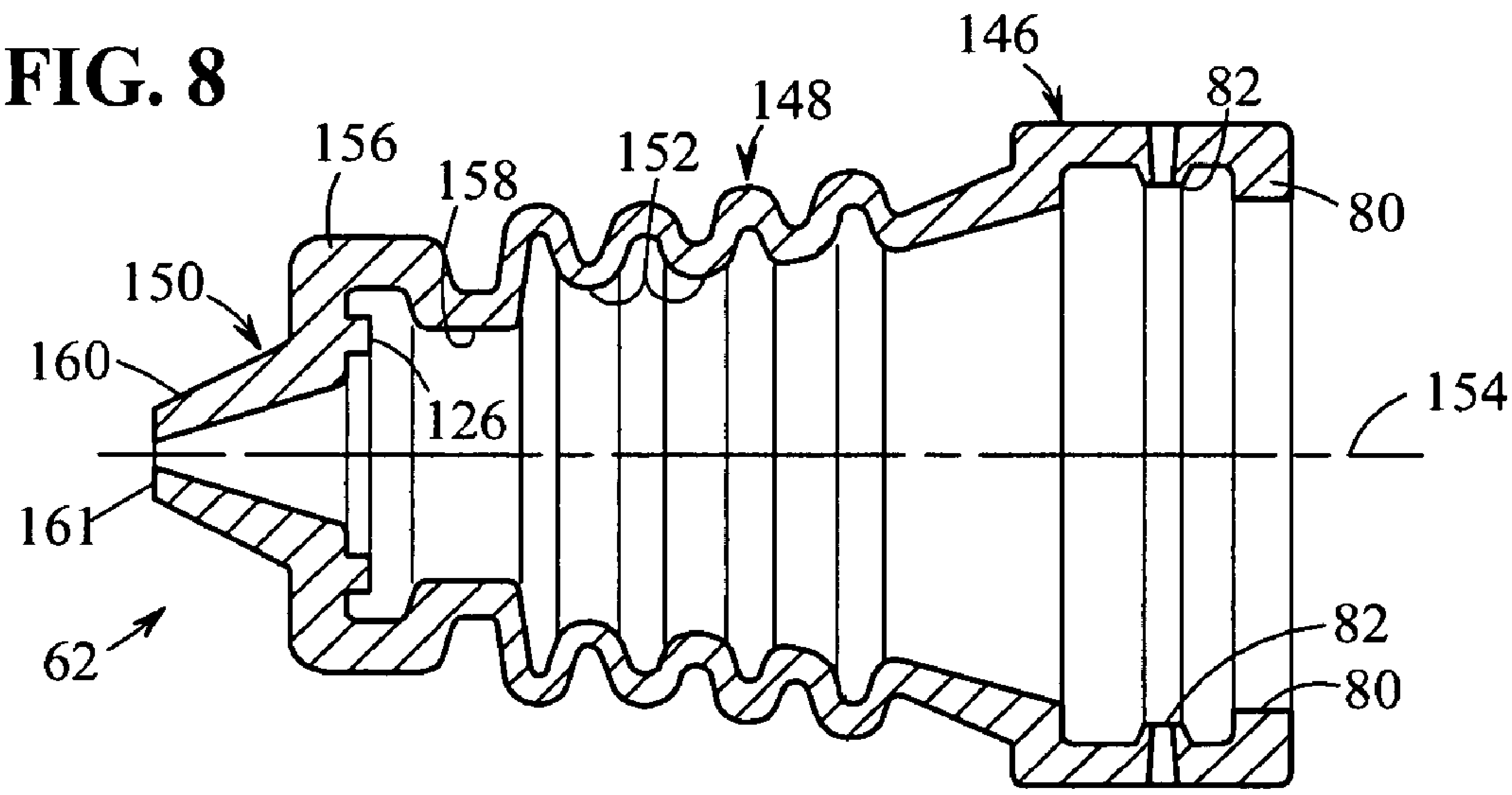

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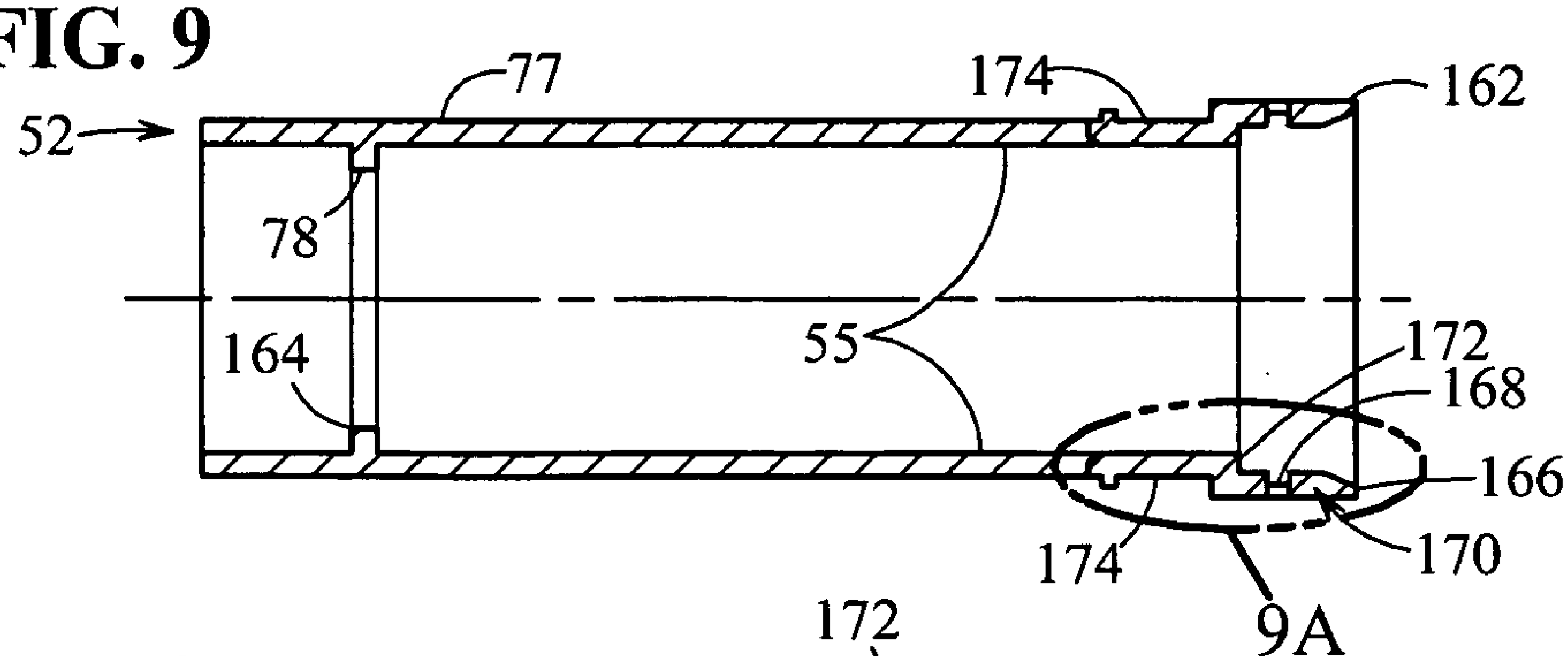
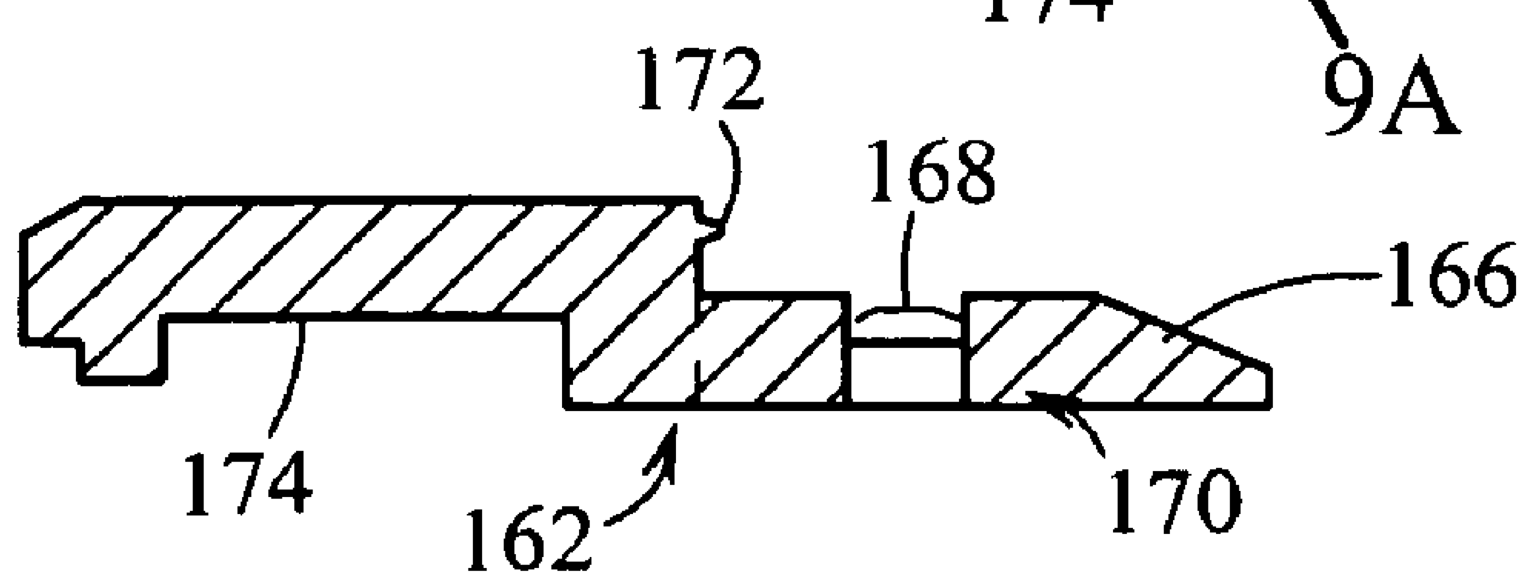
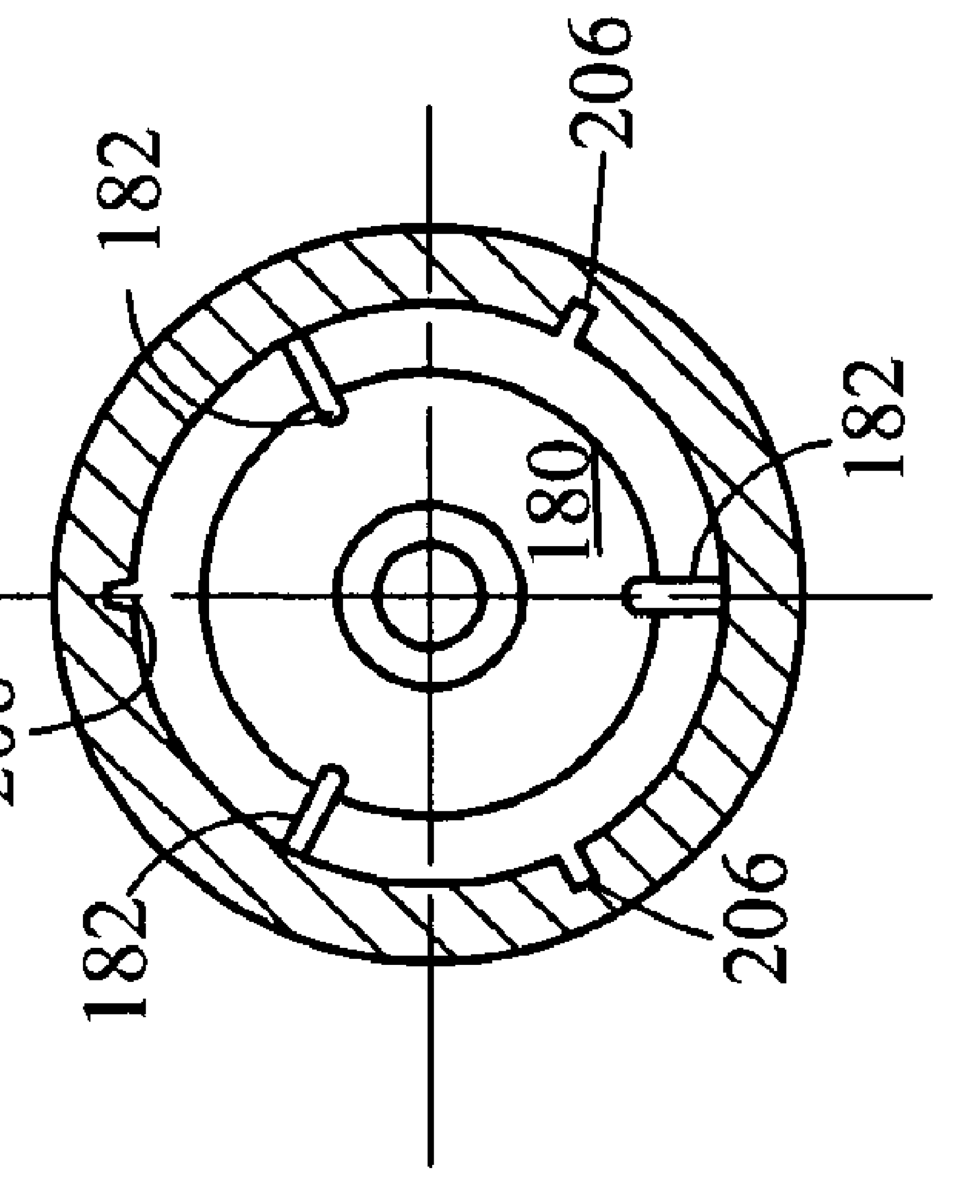


FIG. 9A

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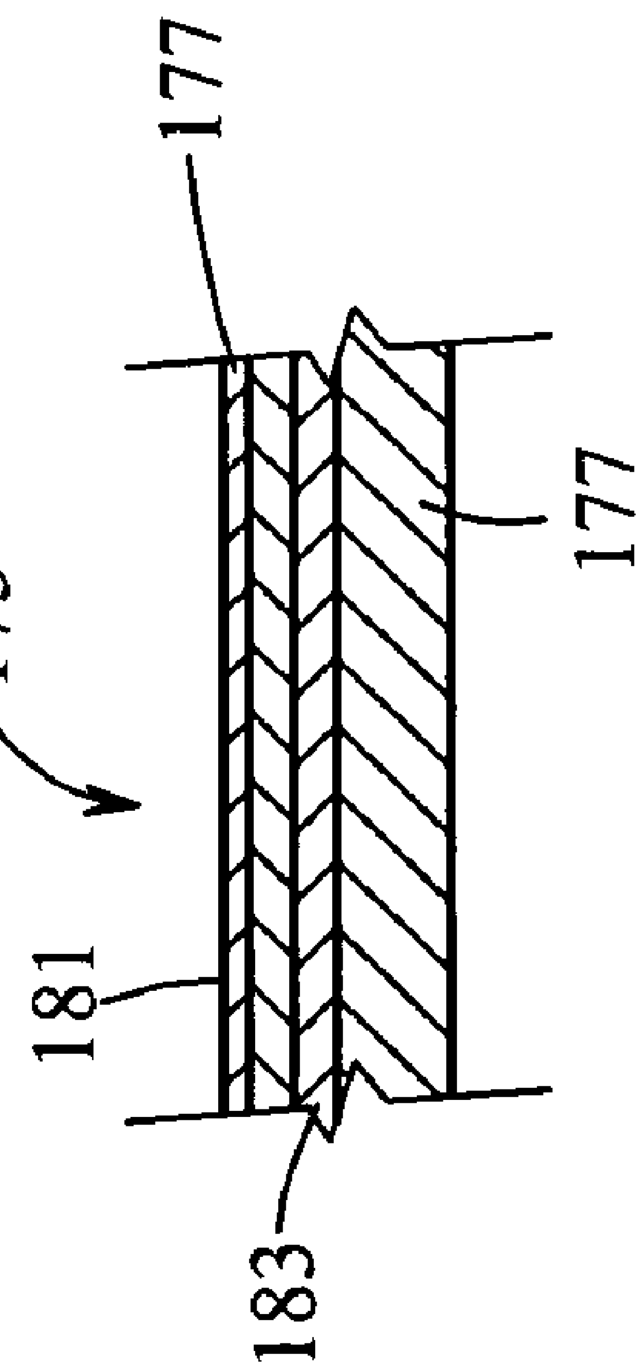
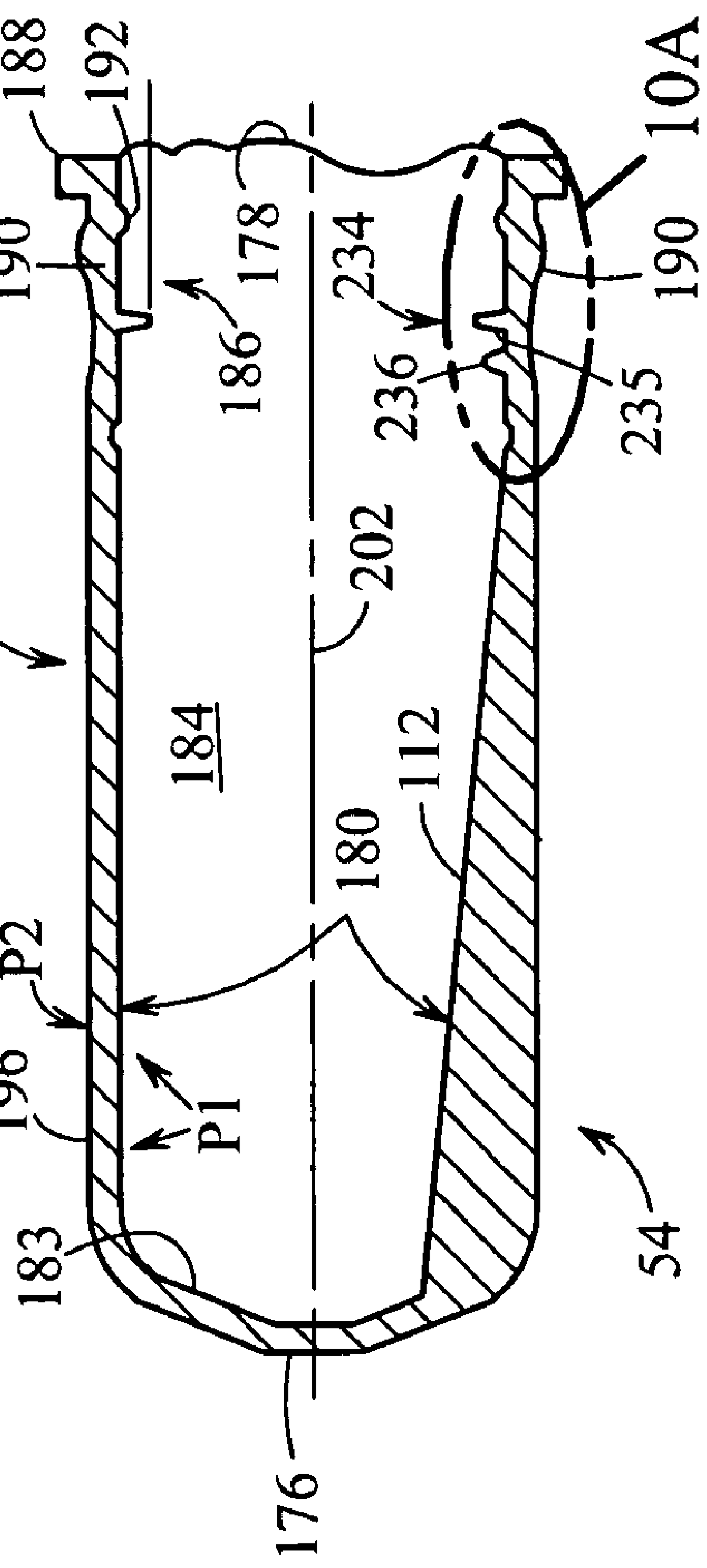


FIG. 10B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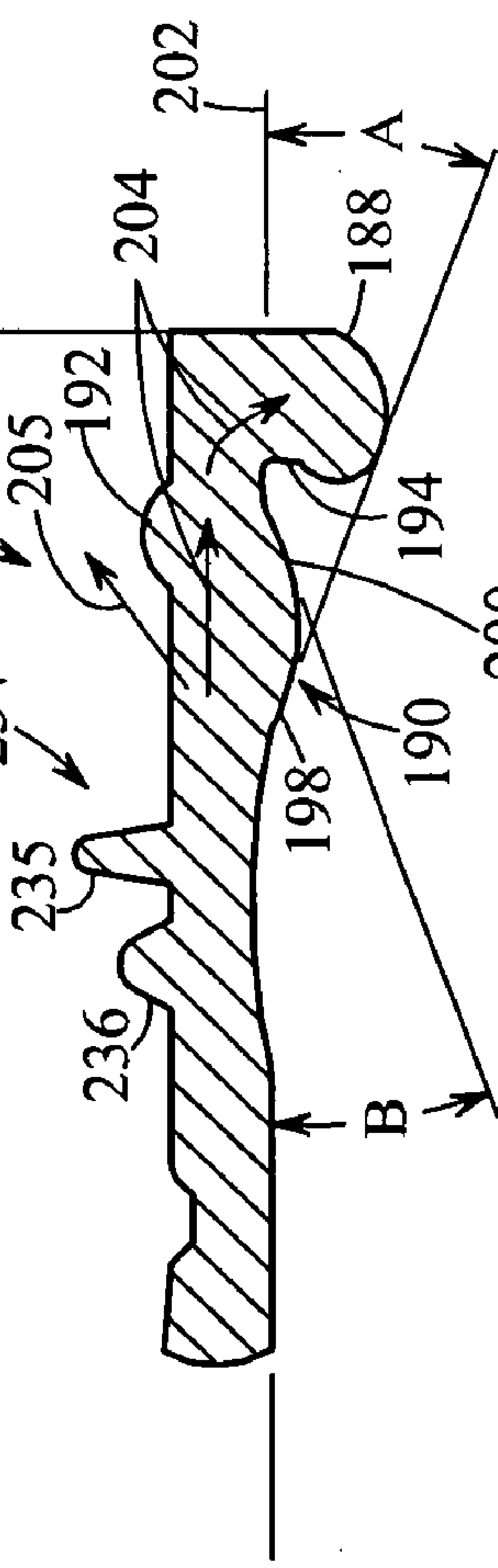
FIG. 10A

FIG. 12

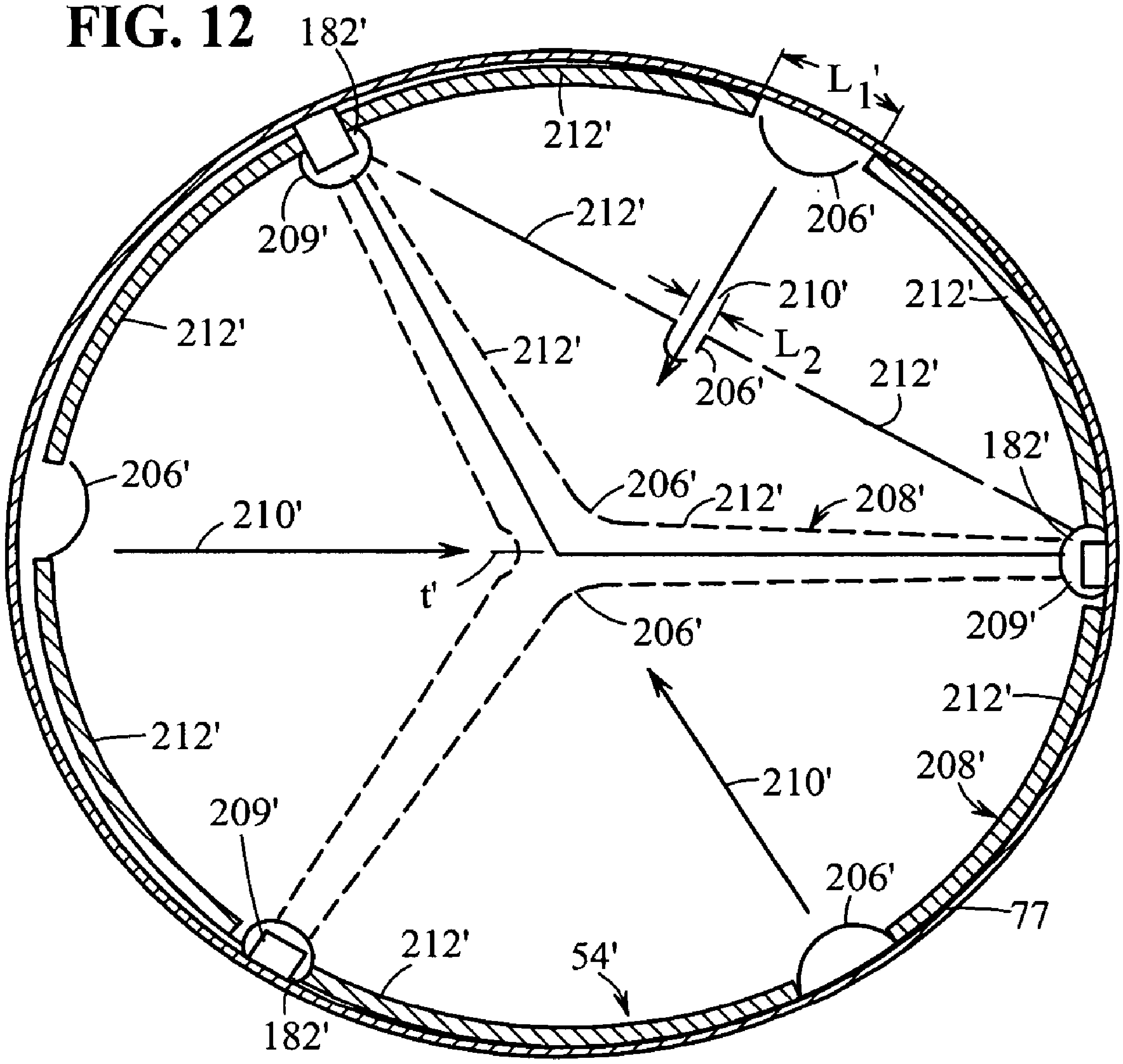
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FIG. 13

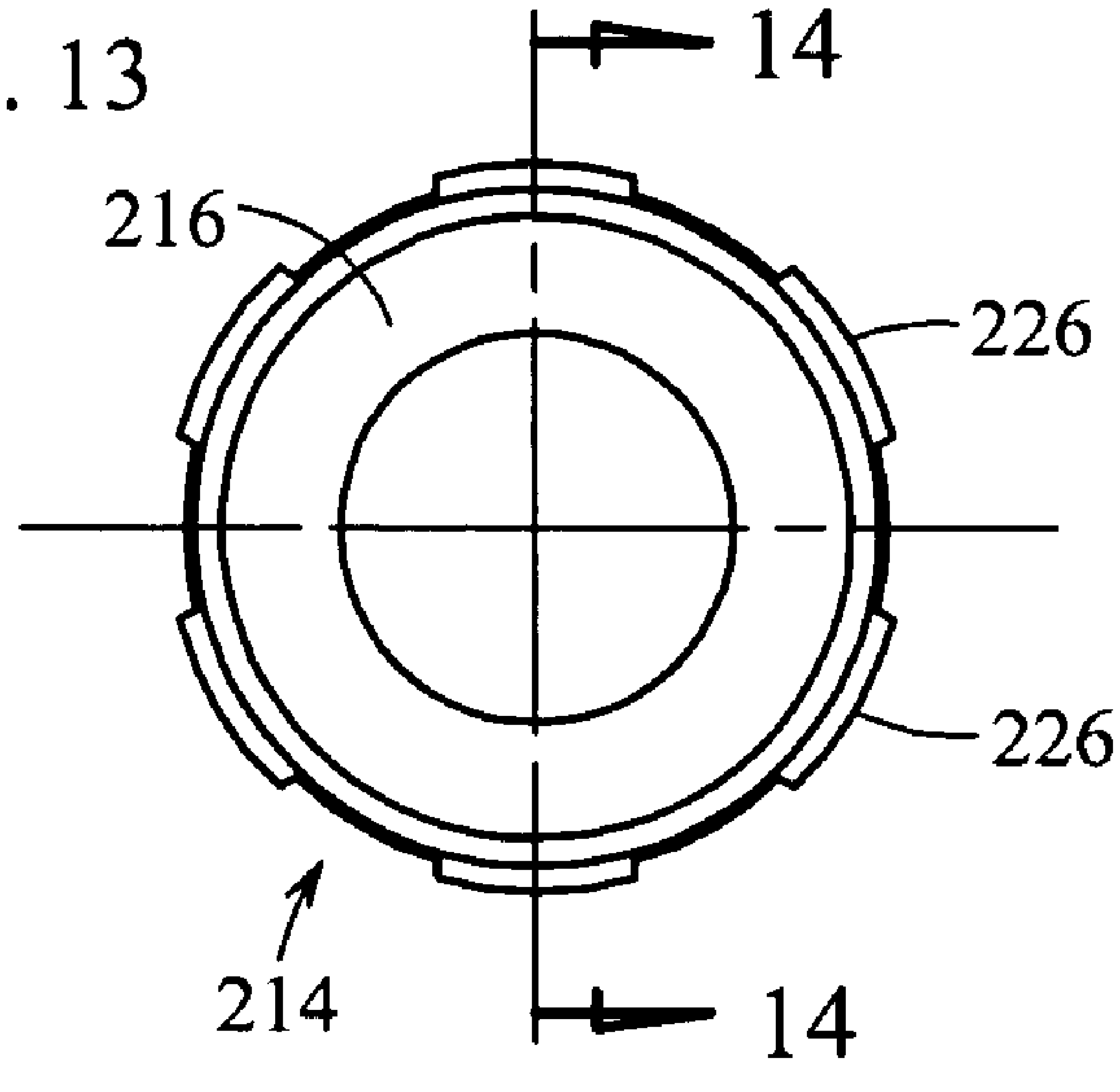


FIG. 14

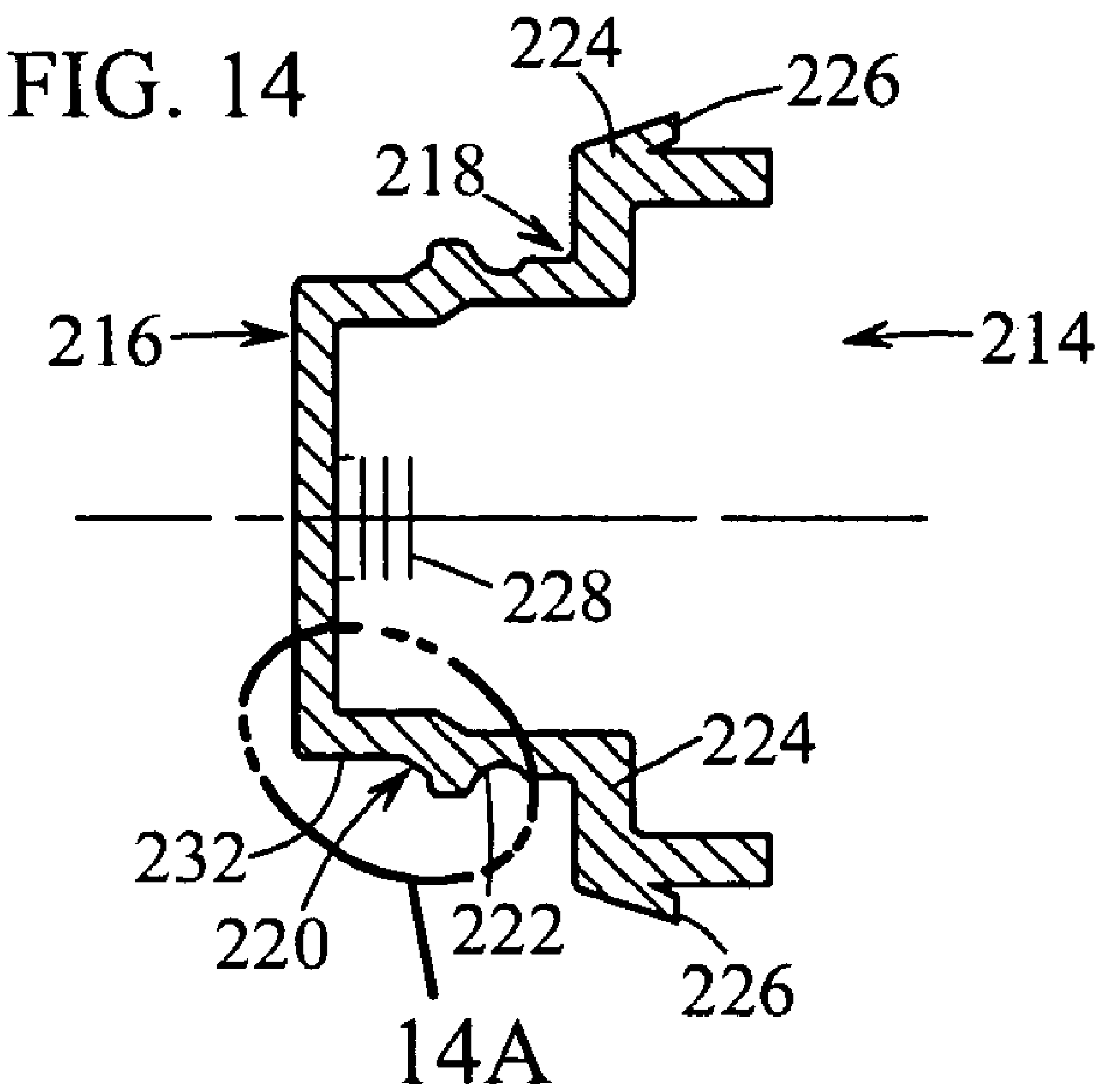
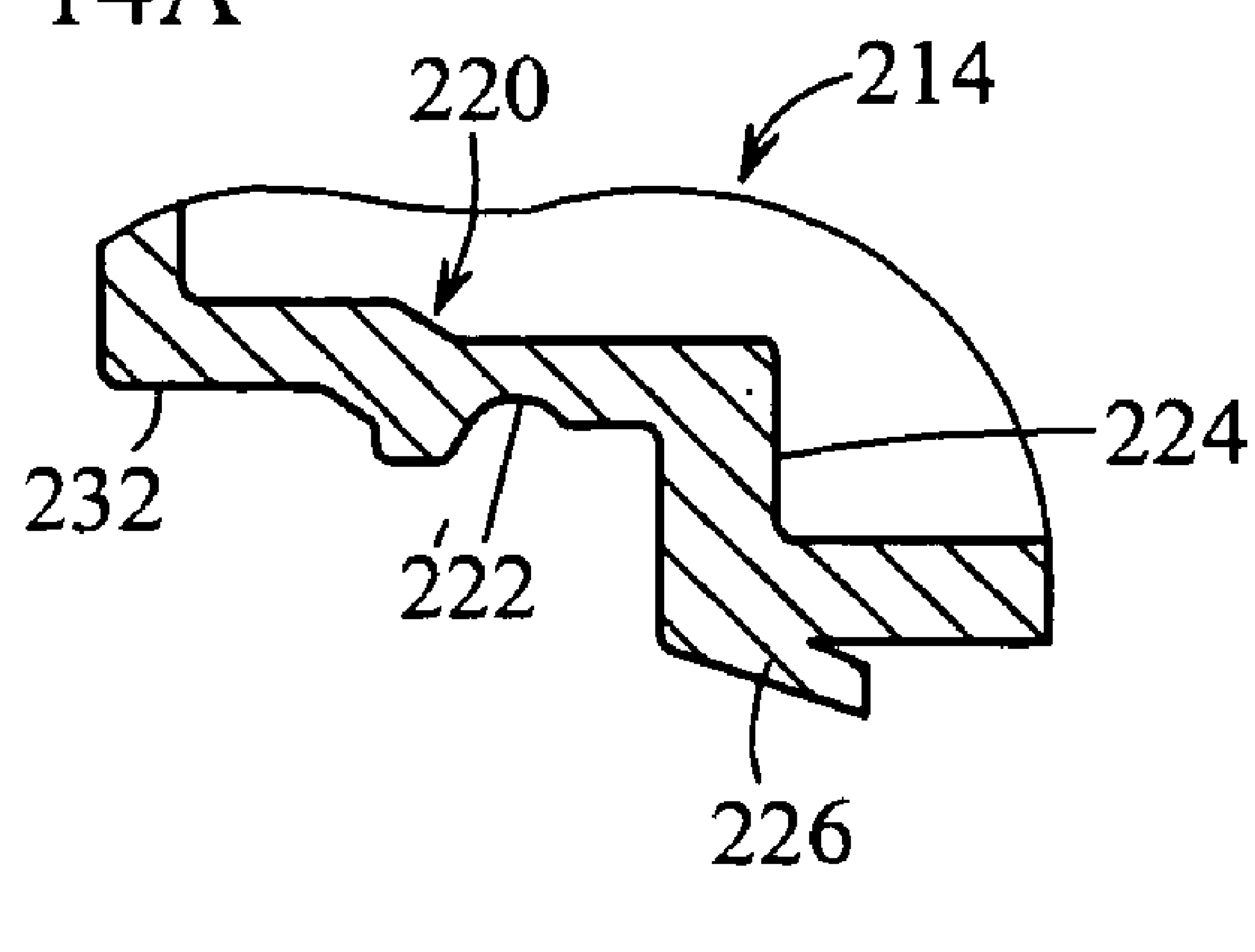


FIG. 14A



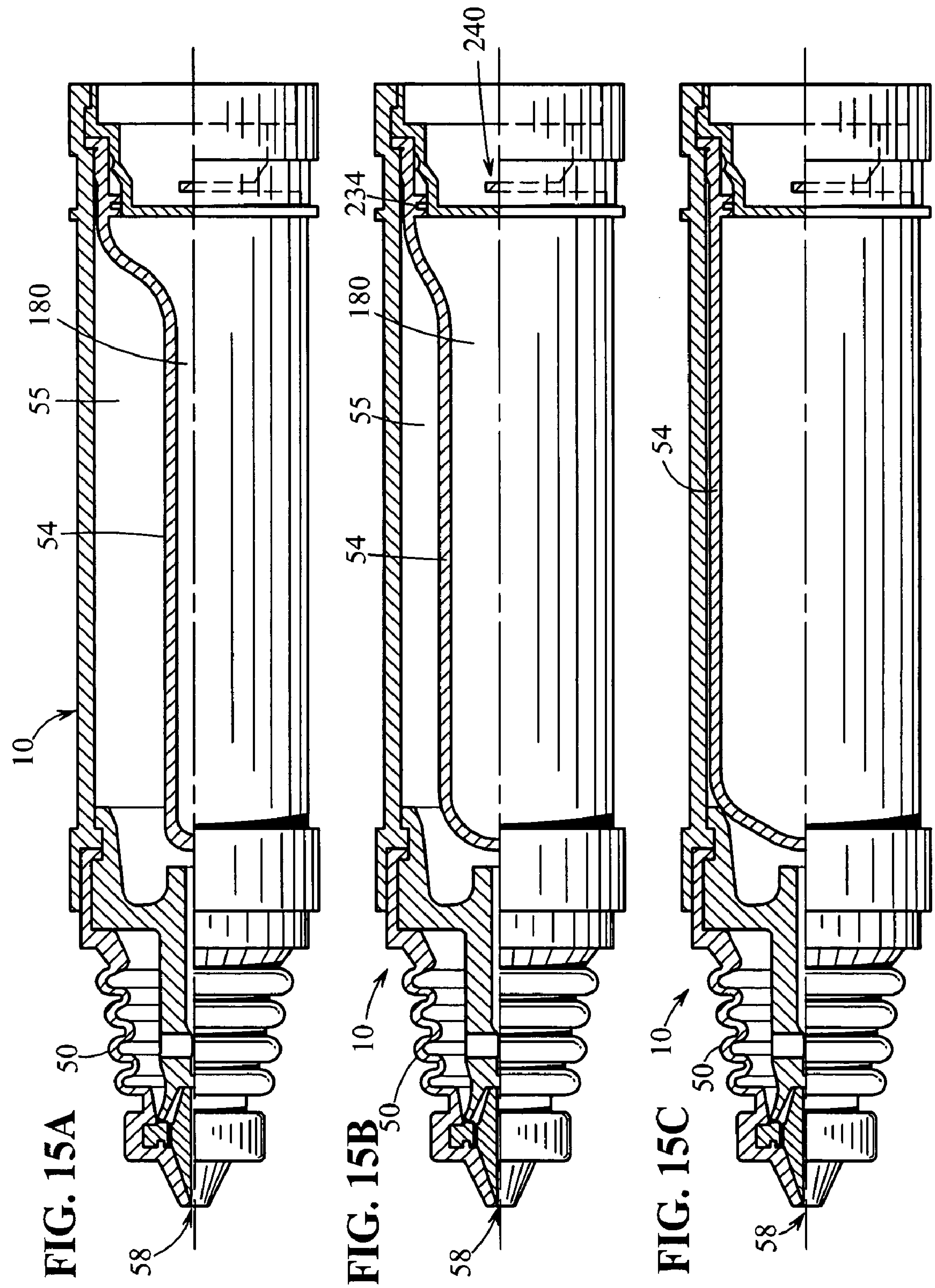


FIG. 15A

FIG. 15B

FIG. 15C

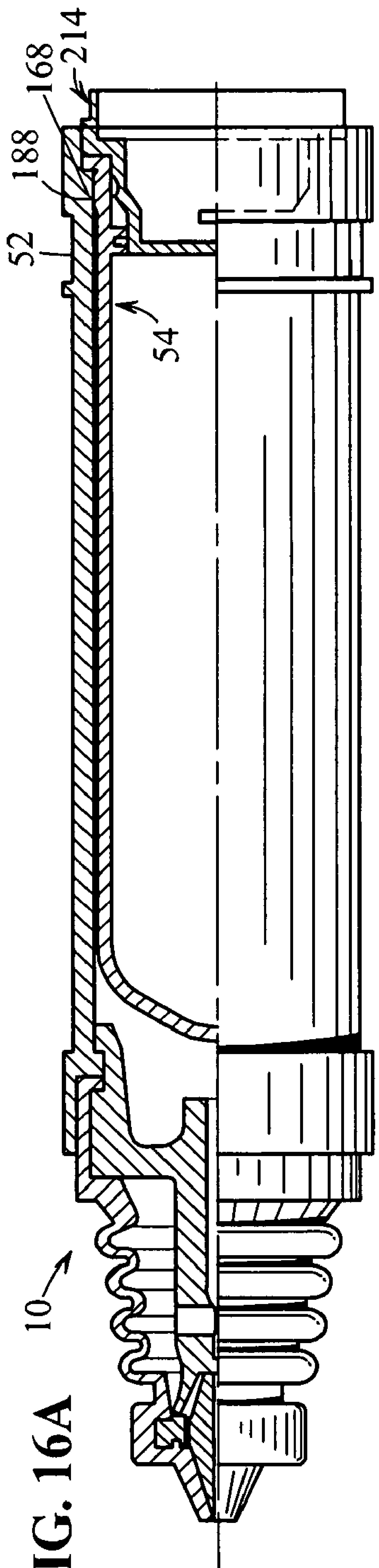


FIG. 16A

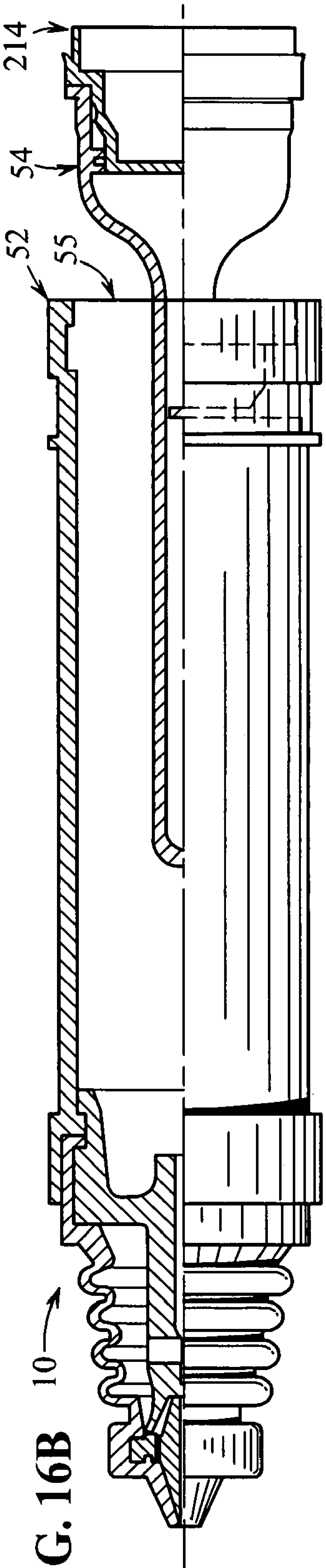


FIG. 16B

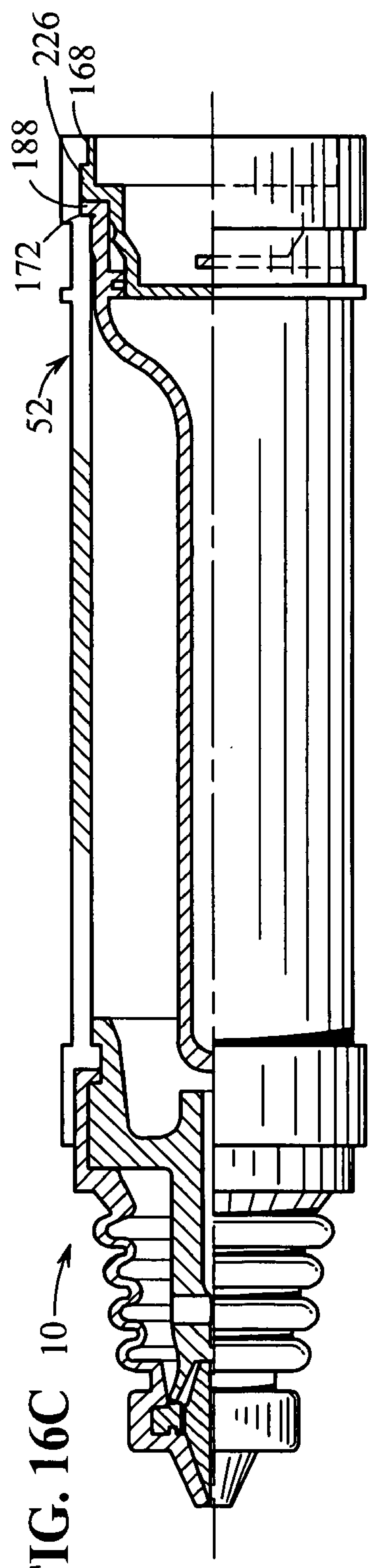


FIG. 16C

FIG. 17

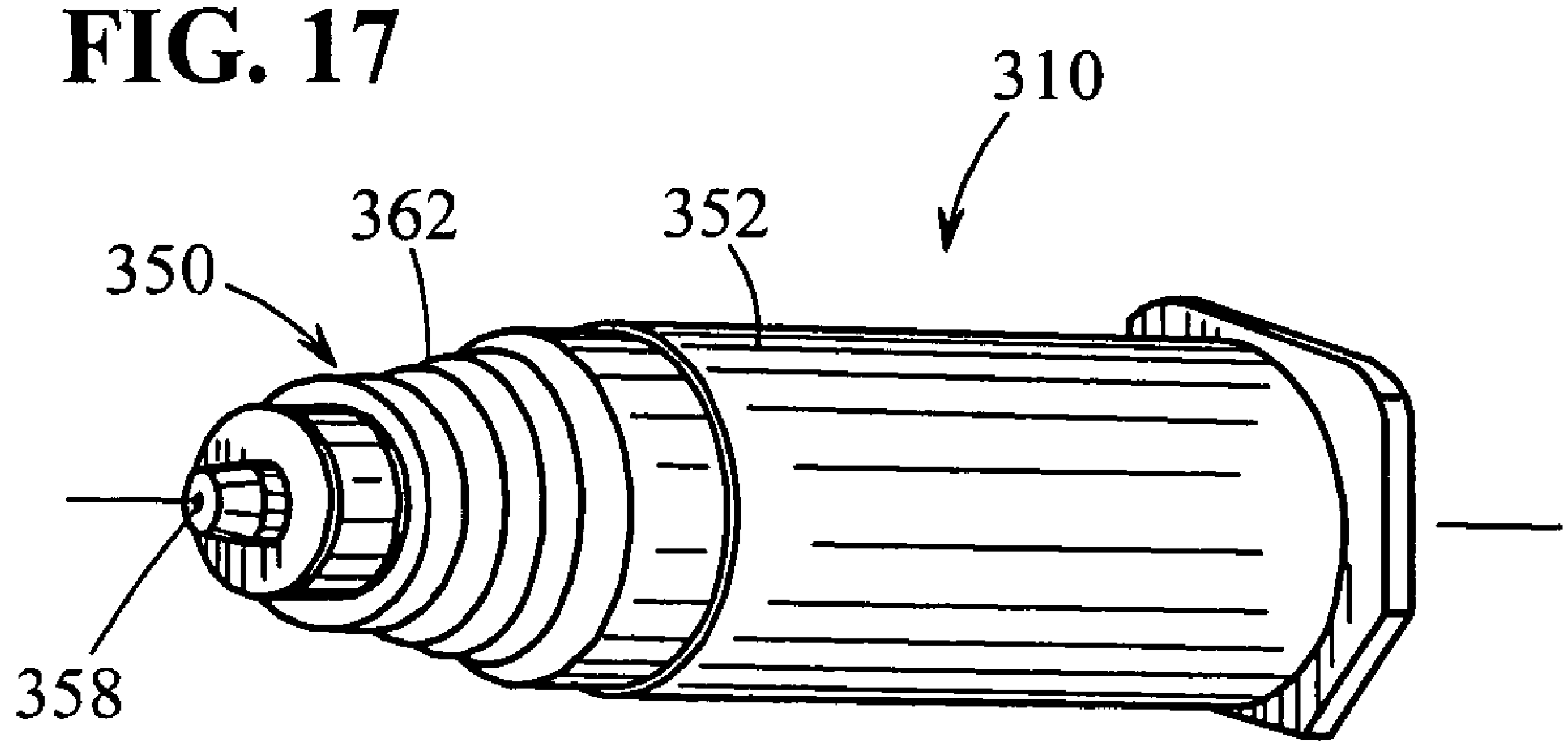
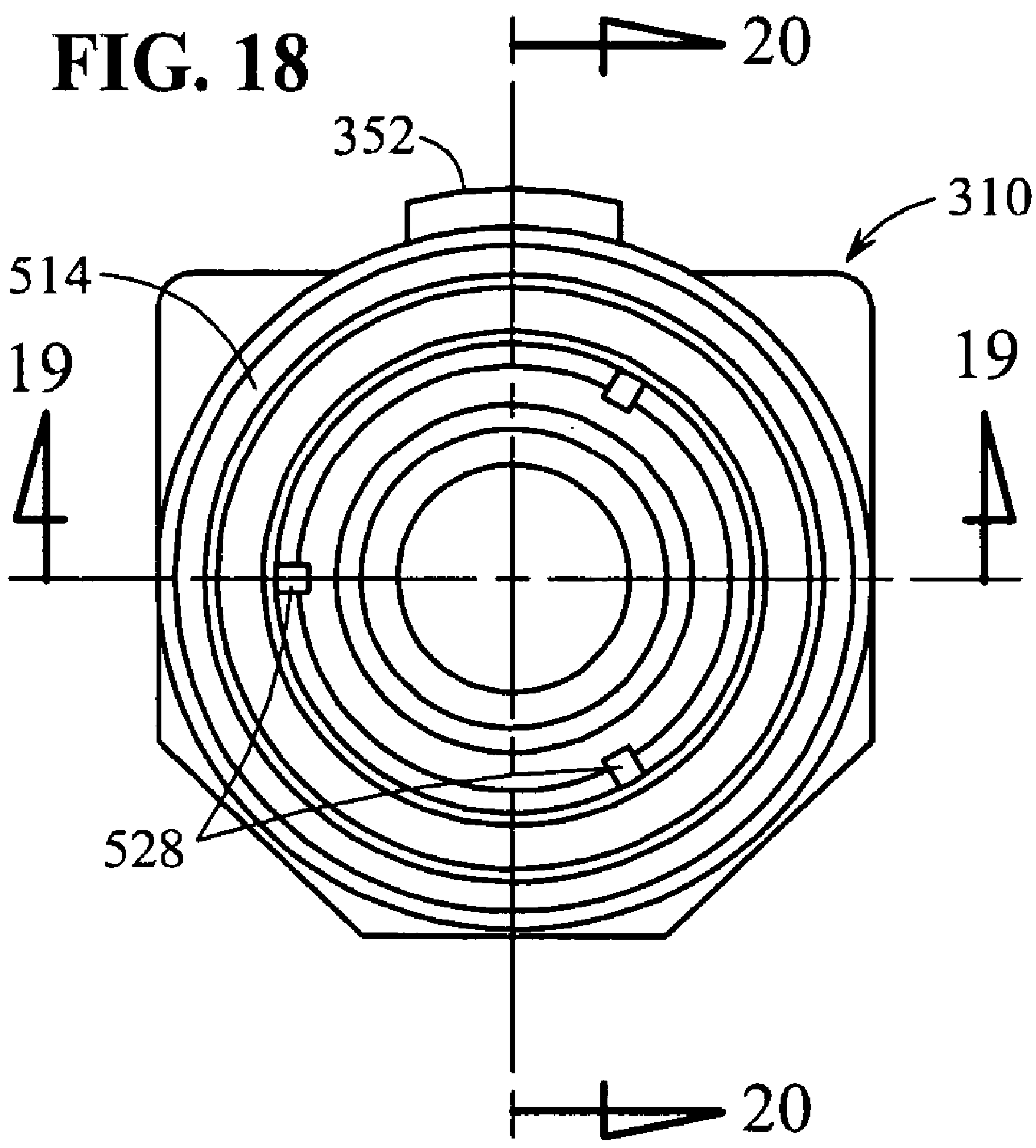


FIG. 18



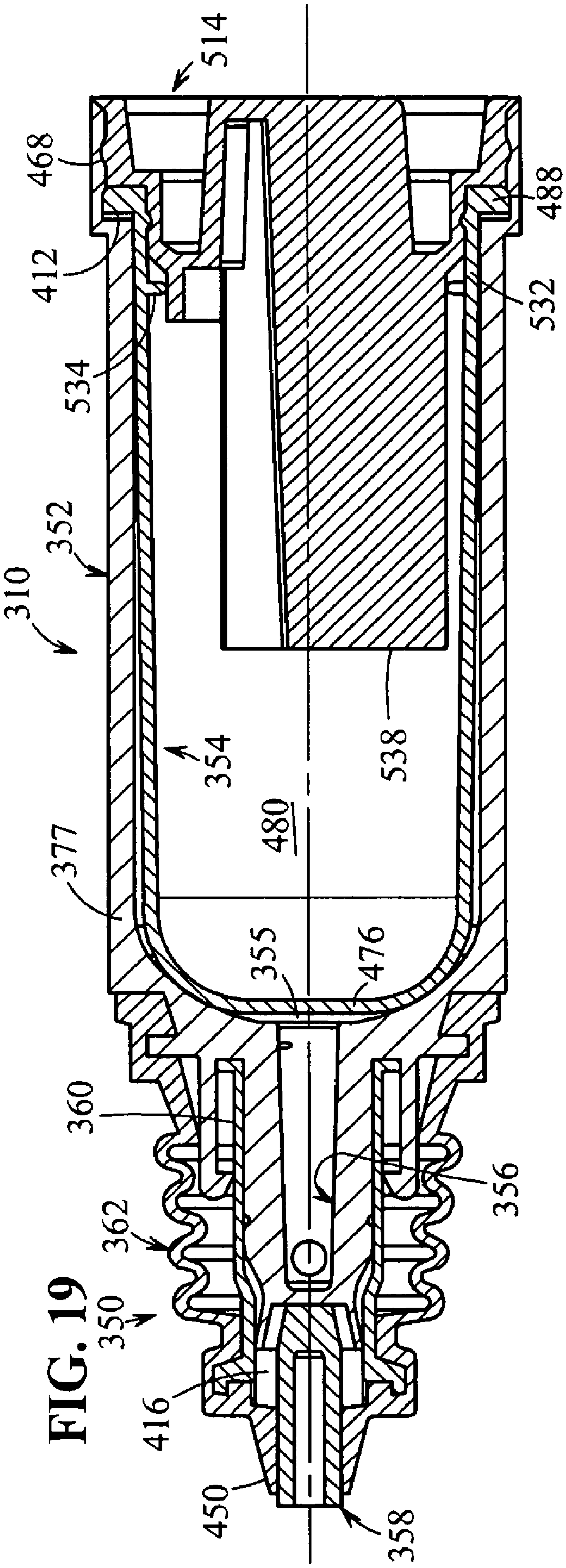

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FIG. 19

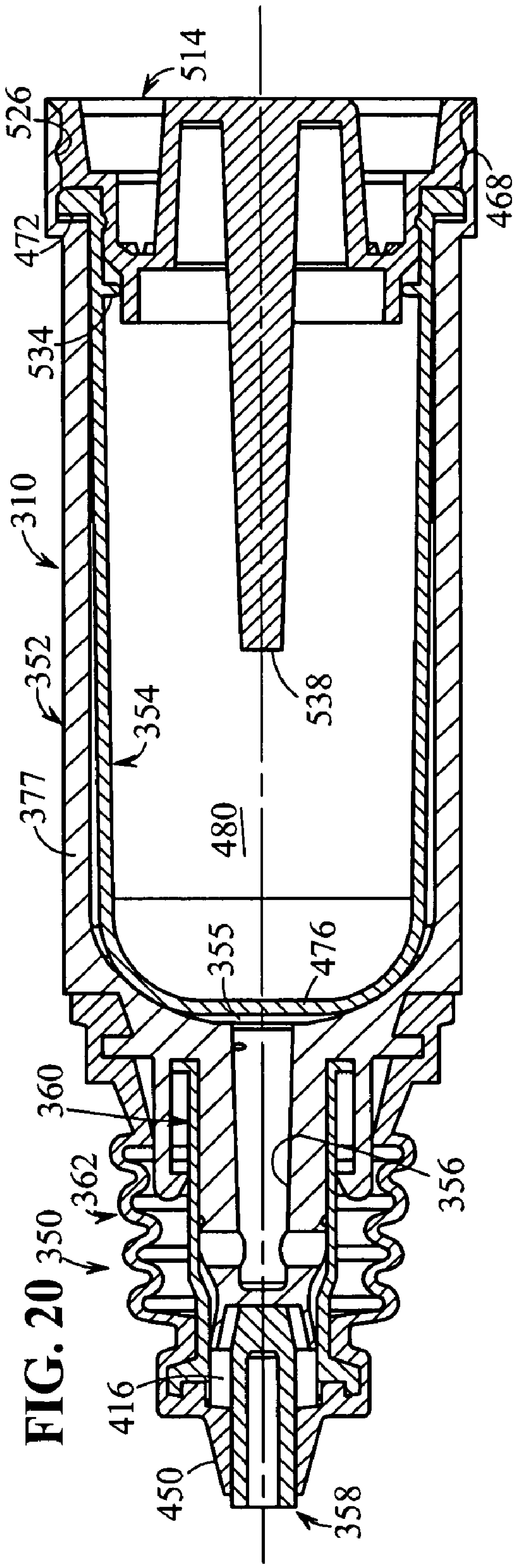
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FIG. 20

FIG. 21

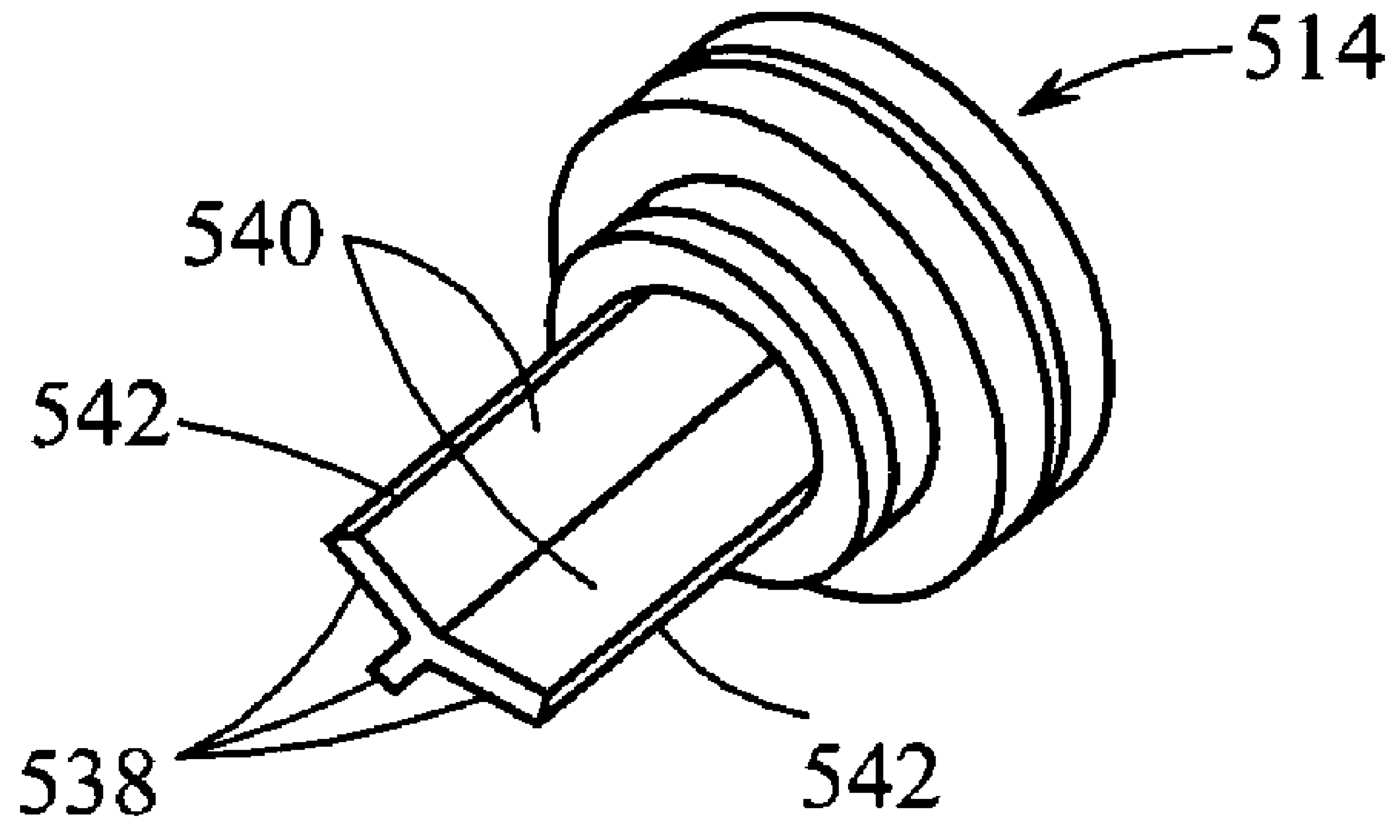

FIG. 22

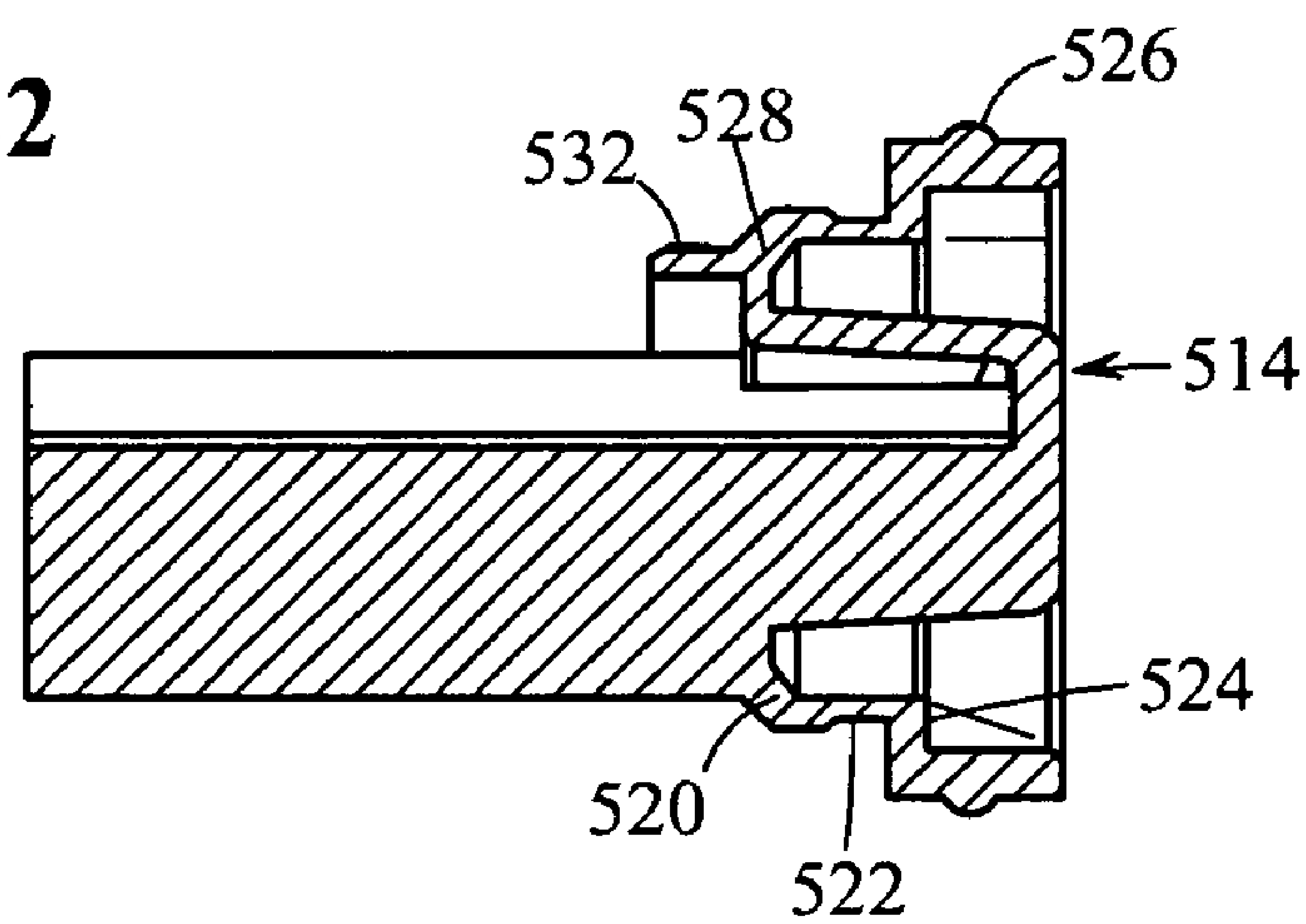

FIG. 23

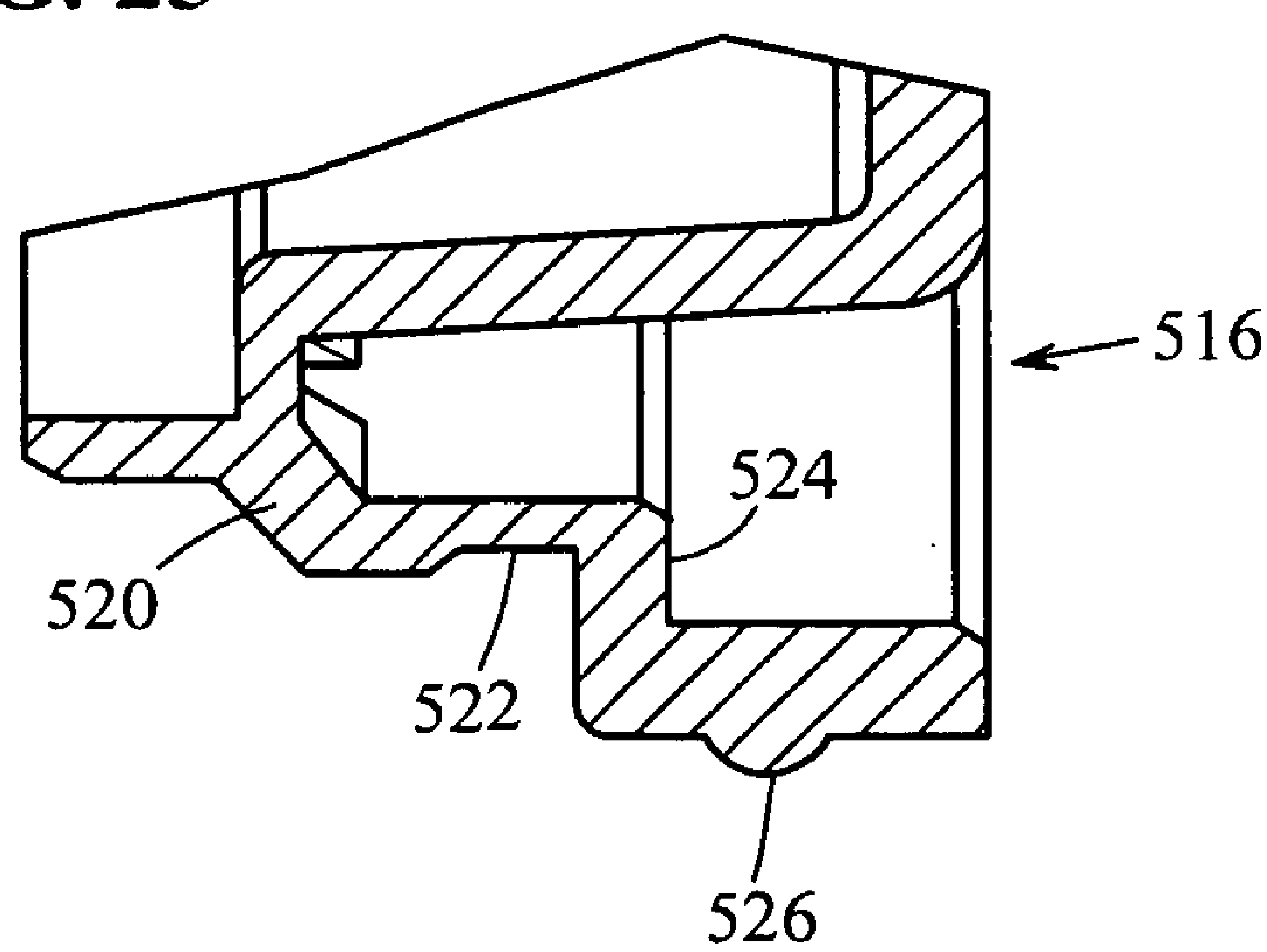

FIG. 24

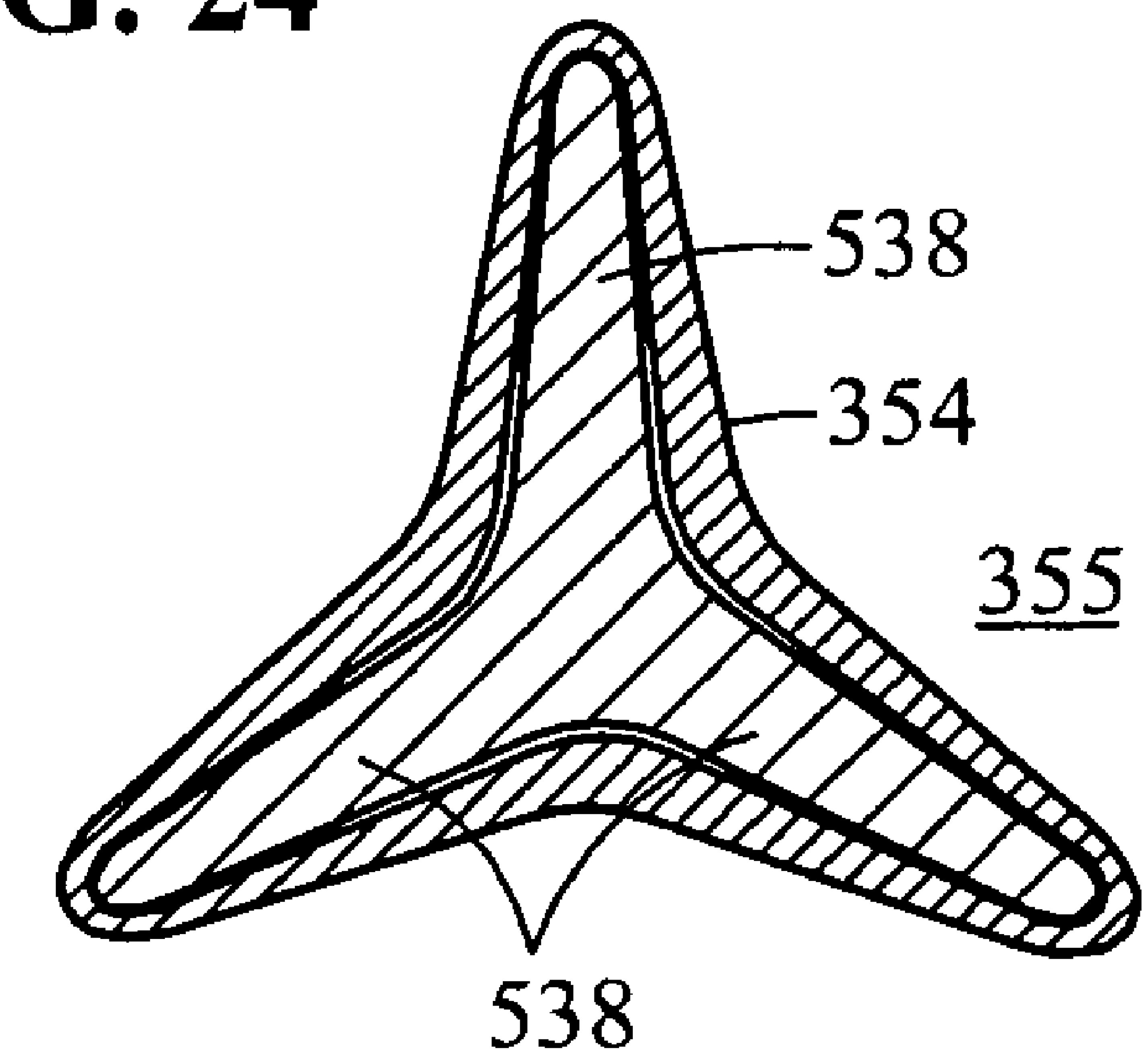

FIG. 25

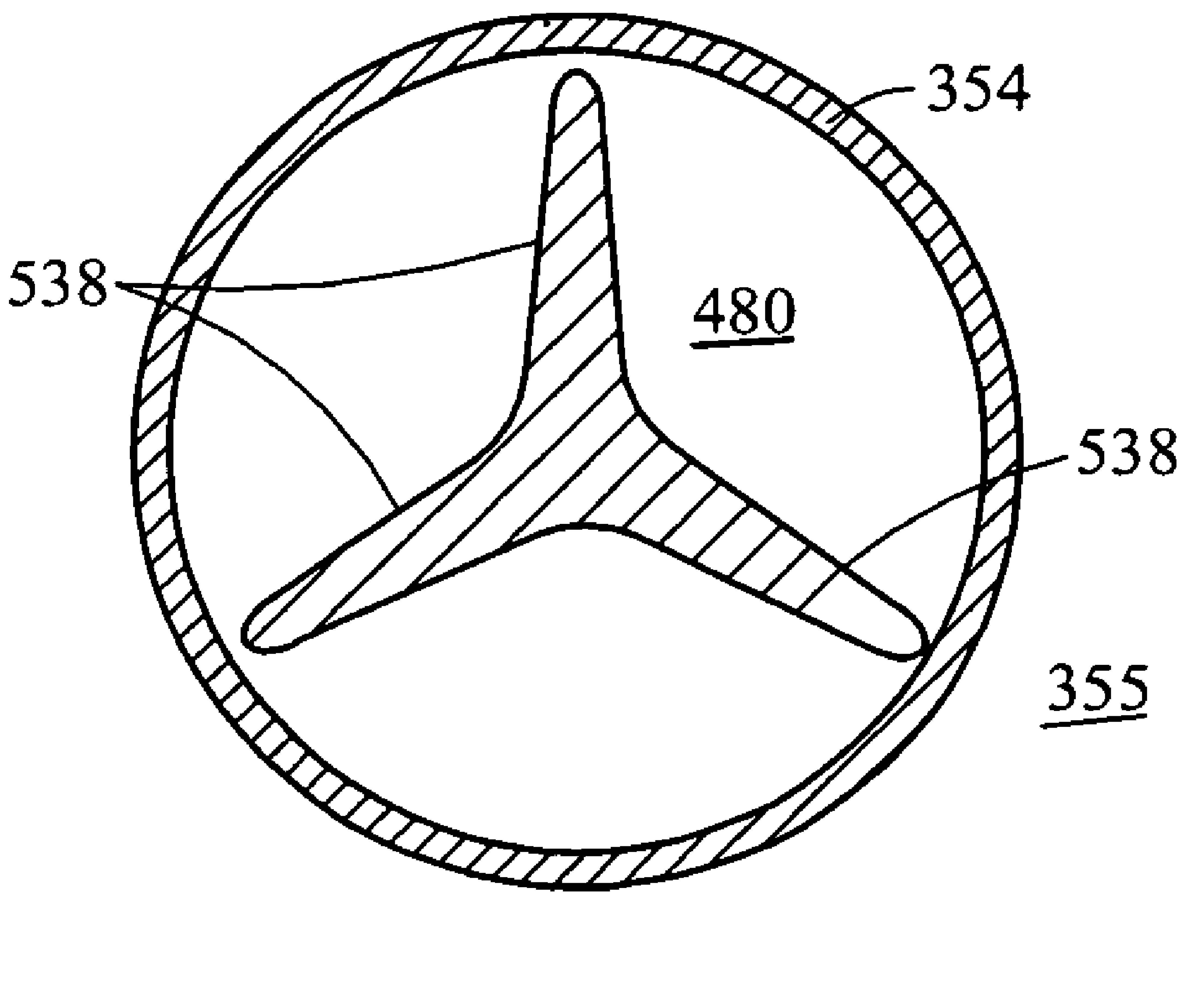

FIG. 26

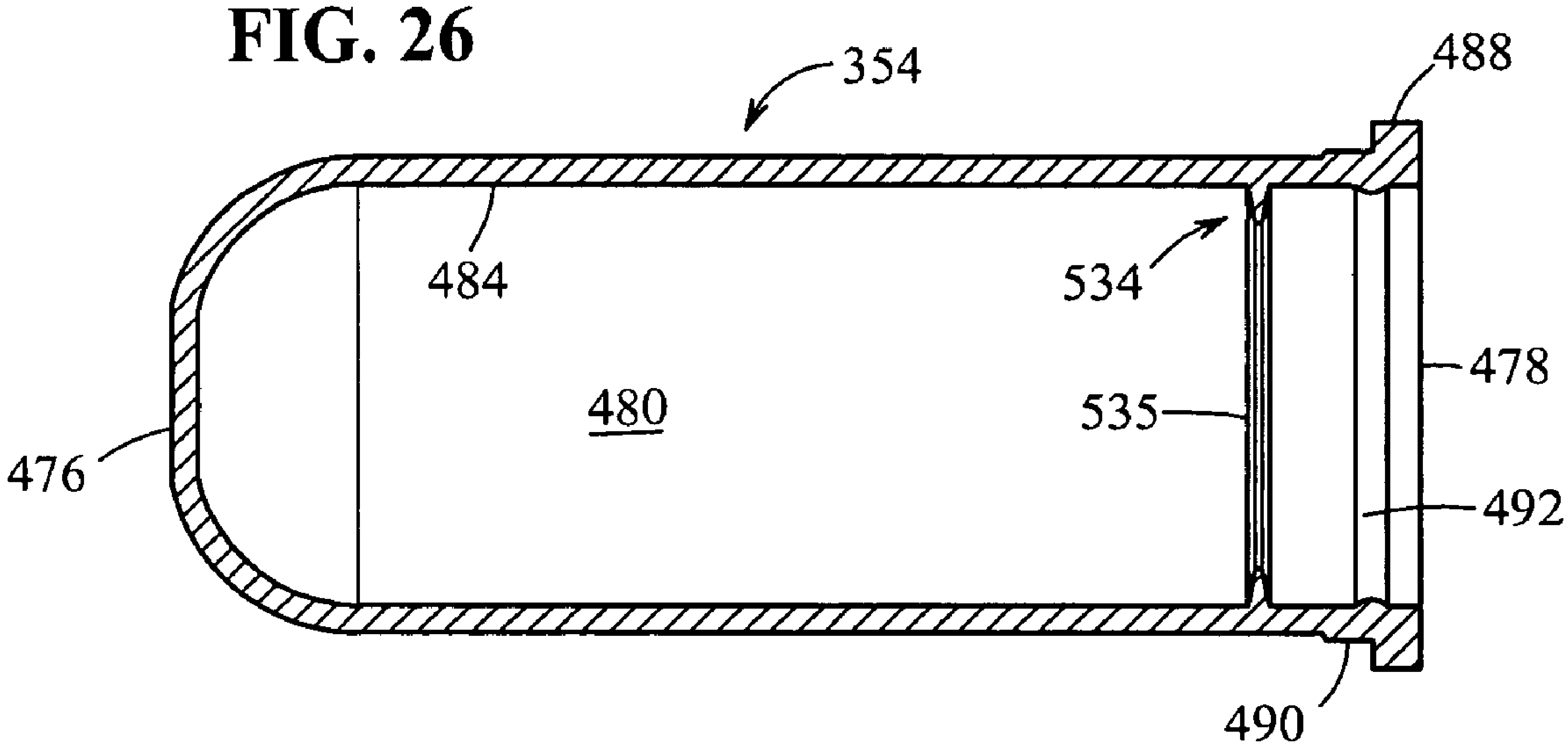
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FIG. 27

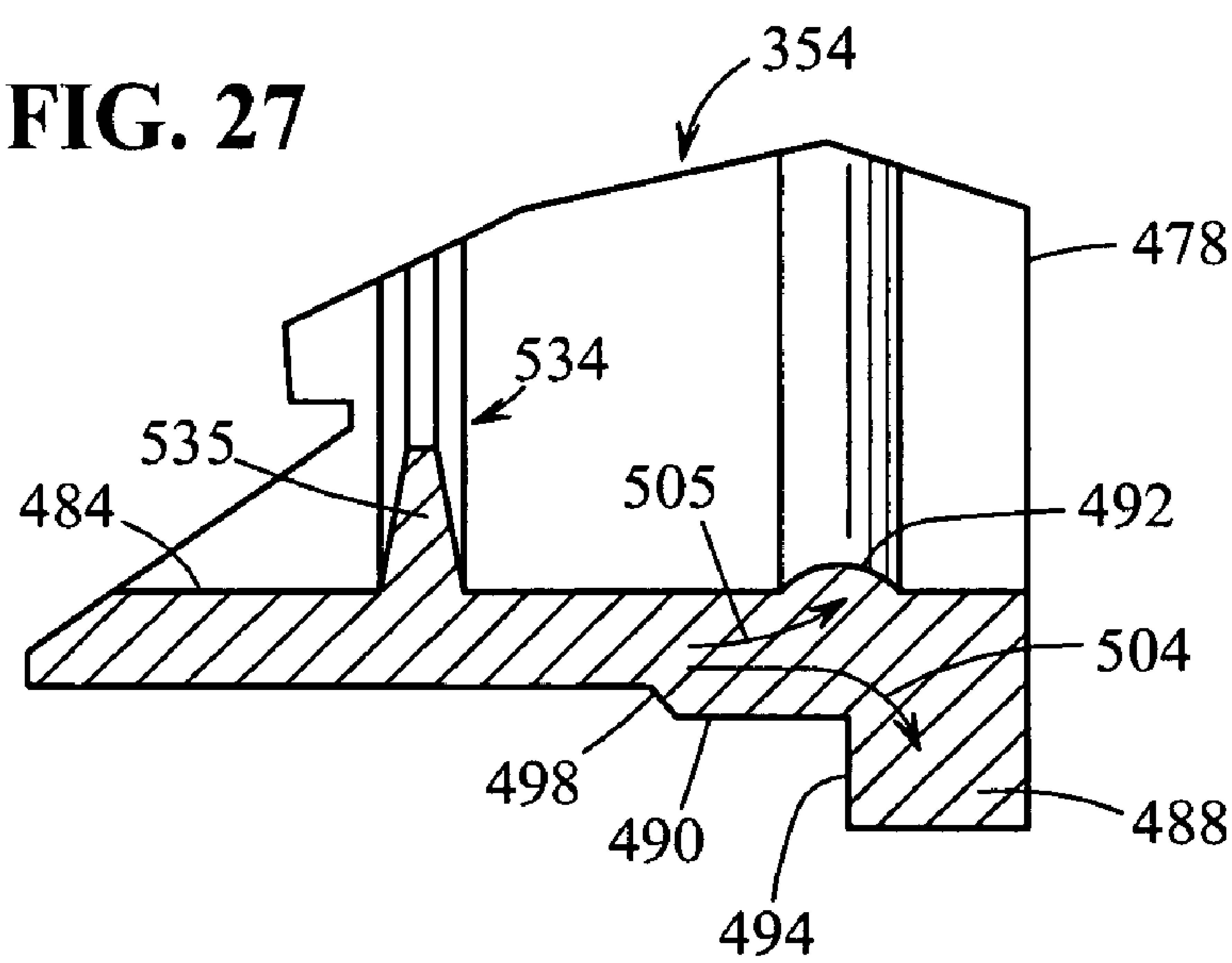
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FIG. 28

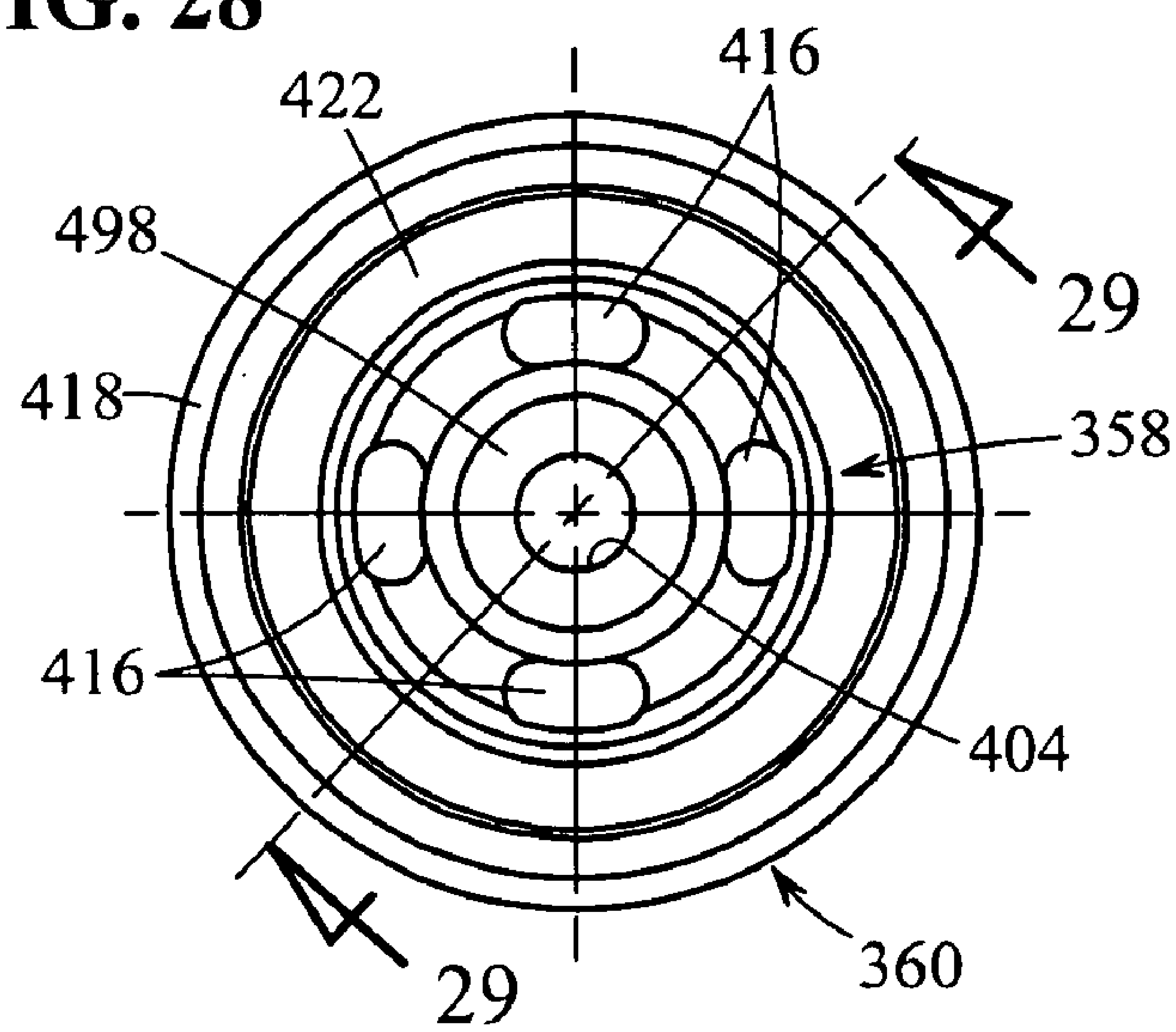
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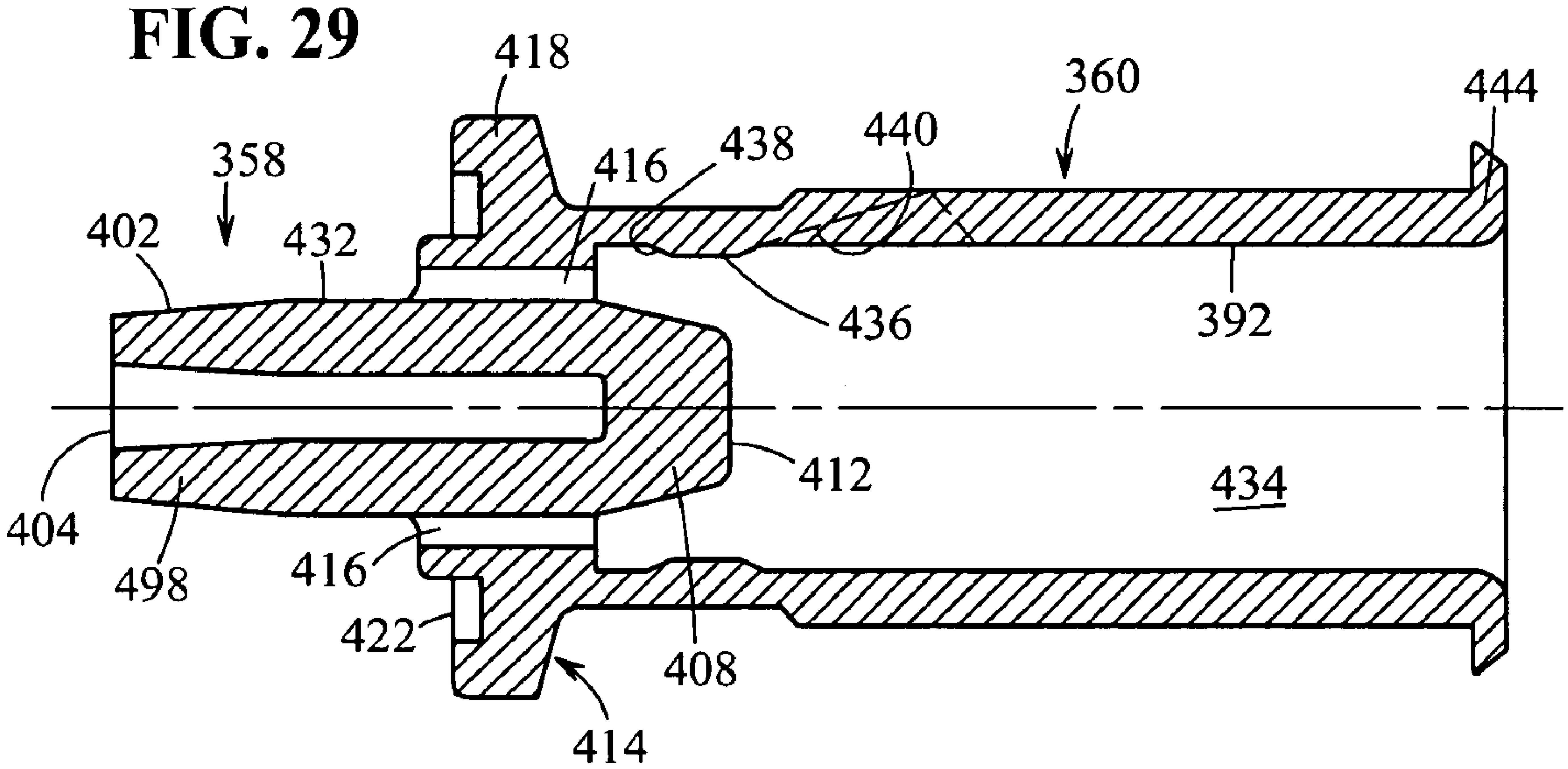
FIG. 29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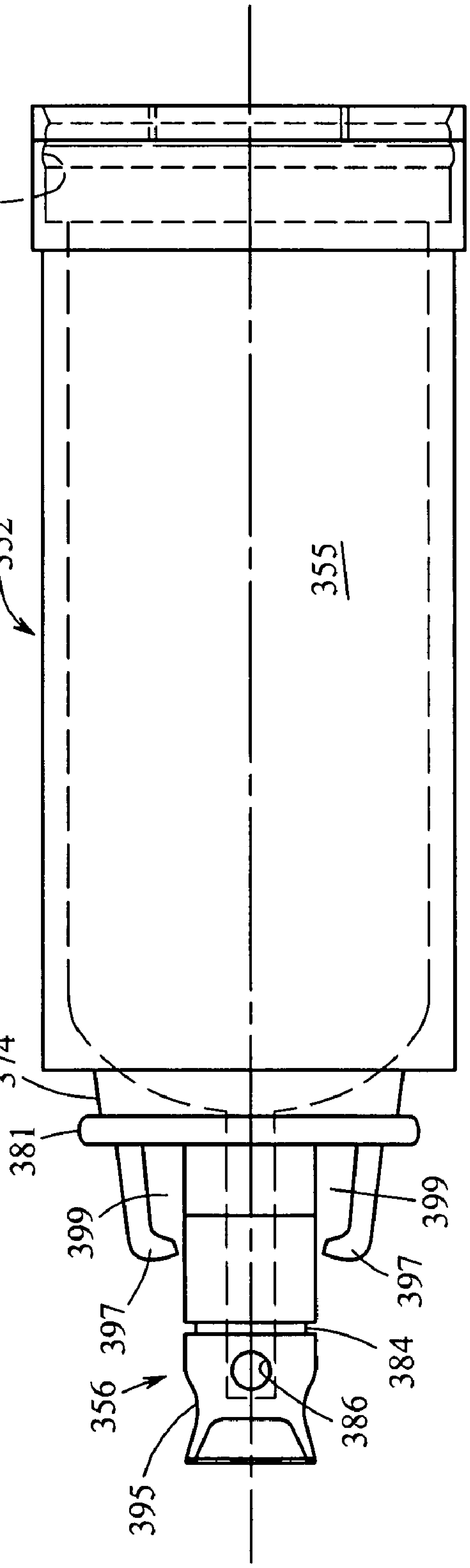
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FIG. 30

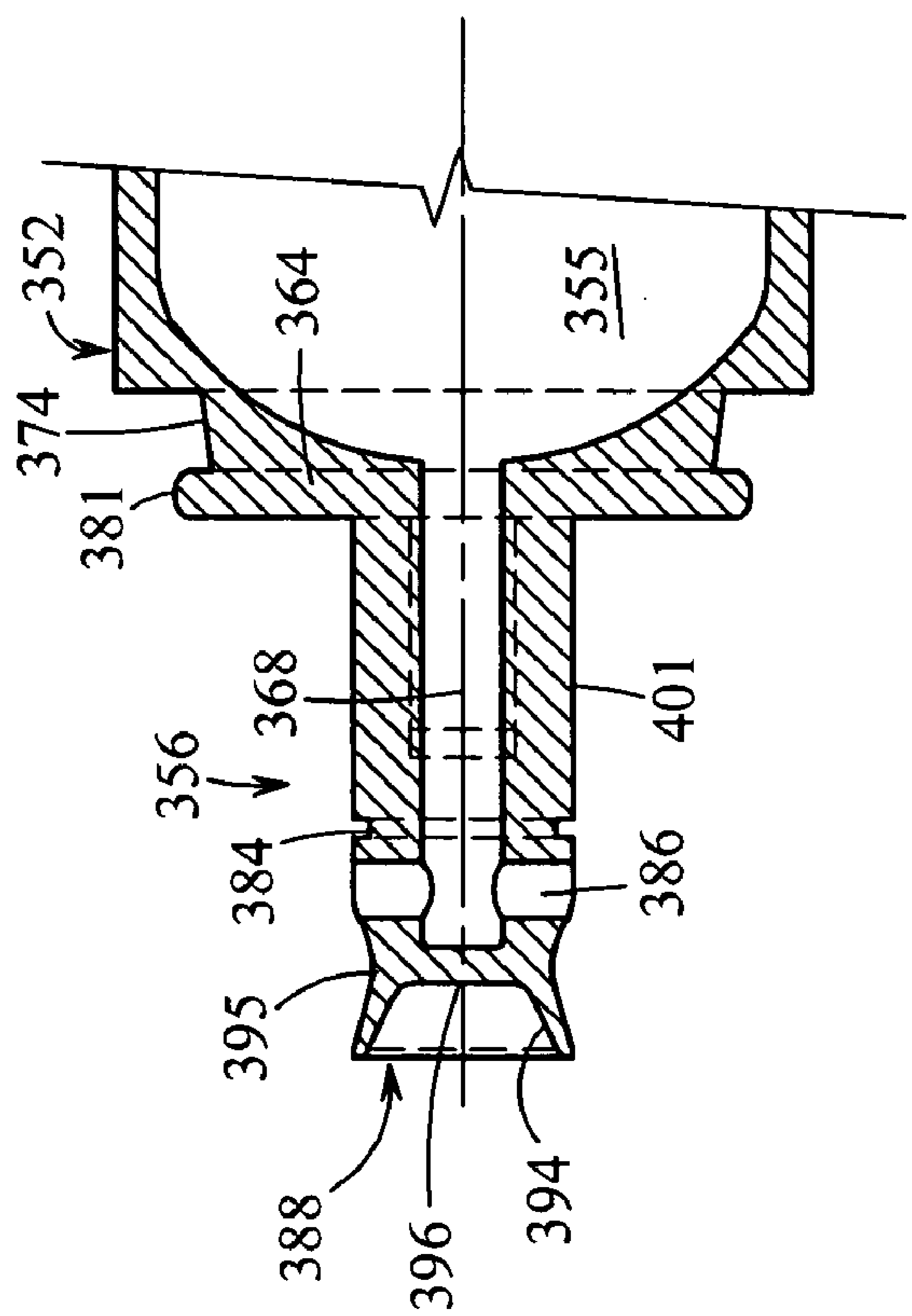
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FIG. 31

FIG. 32

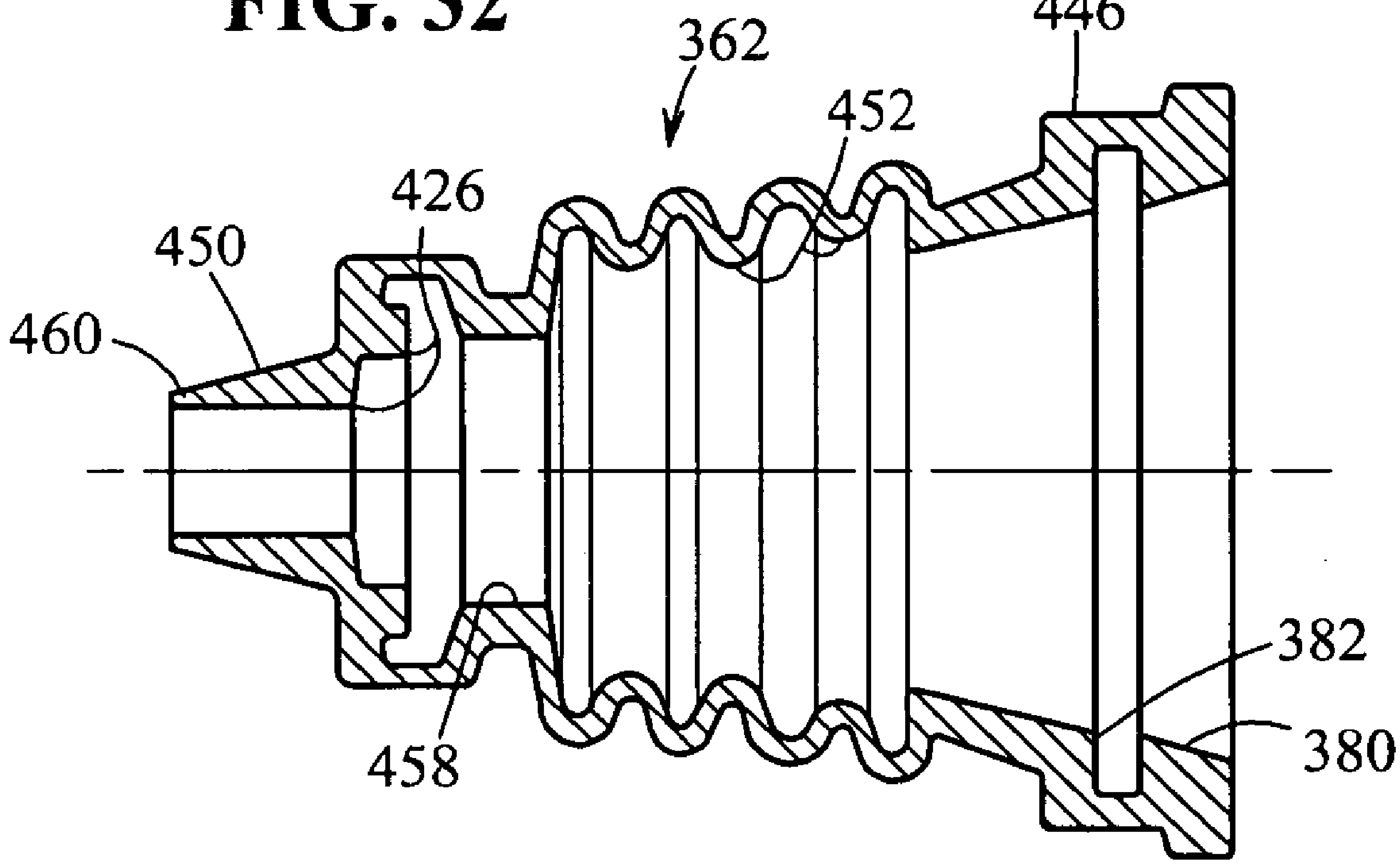
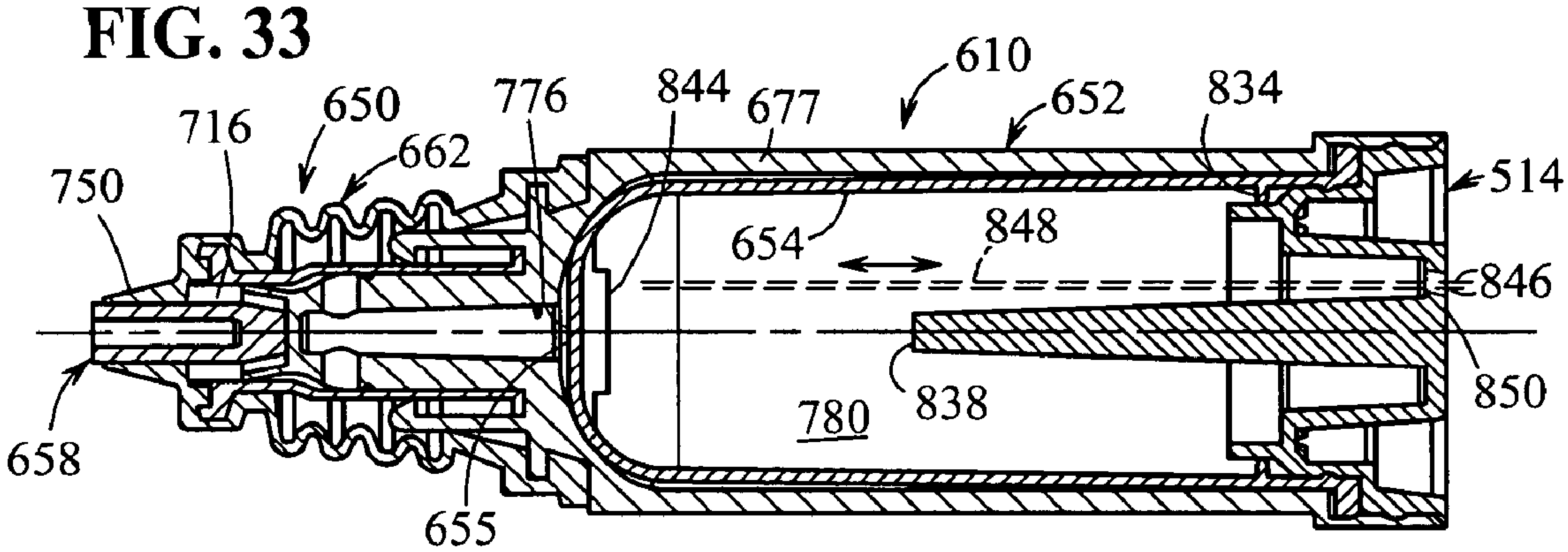


FIG. 33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FLUID DISPENSER HAVING A ONE-WAY VALVE, PUMP, VARIABLE-VOLUME STORAGE CHAMBER, AND A NEEDLE PENETRABLE AND LASER RESEALABLE PORTION

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation of U.S. patent application Ser. No. 10/890,465, filed Jul. 12, 2004, now U.S. Pat. No. 7,000,806, entitled "Fluid Dispenser Having a One Way Valve, Pump, Variable-Volume Storage Chamber, and a Needle Penetrable and Laser Resealable Portion", which is a continuation of U.S. patent application Ser. No. 10/001,745, filed Oct. 23, 2001, now U.S. Pat. No. 6,761,286, entitled "Fluid Dispenser Having a Housing and Flexible Inner Bladder", which claims the benefit of U.S. Provisional Application Ser. No. 60/242,595, filed Oct. 23, 2000, entitled "Fluid Dispenser Having A Rigid Vial And Flexible Inner Bladder", and U.S. Provisional Application Ser. No. 60/242,974, filed Oct. 24, 2000, entitled "Fluid Dispenser Having A Rigid Vial And Flexible Inner Bladder", all of which are hereby incorporated by reference as part of the present disclosure.

FIELD OF THE INVENTION

The present disclosure relates generally to dispensers for dispensing fluids or other substances and, more particularly, to a dispenser having a rigid vial, a flexible bladder disposed within the rigid vial and defining a chamber between the flexible bladder and rigid vial for receiving therein a fluid or other substance, and a nozzle and pump assembly coupled in fluid communication with chamber for dispensing fluids or other substances therefrom.

BACKGROUND INFORMATION

Typical fluid dispensers include a container defining therein a chamber for receiving a fluid to be dispensed, a nozzle and pump assembly mounted on the container, and a dip tube extending downwardly from the nozzle into the chamber for pumping the fluid from the bottom of the chamber, through the dip tube, and out of the dispenser. Other known dispensers include a vial and a flexible bladder received within the vial. For example, U.S. Pat. No. 6,062,430 to Fuchs shows in FIG. 1 a dispensing container with variable volume compensation including a bottle-shaped vessel 2 in the form of a thin-walled, hollow body made from soft elastic plastic, and a reception container 15 formed of a wrinkle film encapsulated within the vessel body **2**.

One of the drawbacks associated with typical prior art fluid dispensers is that the fluid chamber(s) are not maintained in a substantially airless condition throughout the storage, shelf life and/or usage of the dispenser. For example, the nozzles and/or valves used in typical prior art dispensers frequently are incapable of maintaining the dispenser in a hermetically sealed condition. Such nozzles and/or valves allow the passage of air or other gases therethrough and into contact with the medicament or other substance contained within the fluid chamber(s). In addition, such nozzles and/or valves frequently allow vapor loss therethrough either during the storage, shelf life or usage of the dispensers.

Another drawback associated with prior art dispensers is that the materials of construction may undergo creep that, in turn, causes seals formed within the dispensers to leak. Many medicaments are maintained in storage and/or on store shelves for at least several, and in some instances, many months. During transportation and storage, the dispensers can be subjected to varying atmospheric conditions involving large variations in atmospheric temperature, pressure and/or humidity. As a result, the dispensers are frequently subjected to substantial differential thermal expansion and/or contraction that, in turn, cause the materials of construction to undergo creep. The seals and other components of such prior art dispensers typically are not designed to address such creep, and as a result, the dispensers develop leaks or otherwise allow air ingress and/or vapor loss when subjected to such long periods of storage or varying atmospheric conditions. For example, some polyethylene dispensers have been known to lose between about 10% to 25% of the weight of their contents during storage. Such weight loss is believed to be due to vapor loss from the medicament or other fluid-containing chambers through the polyethylene walls of the dispensers and/or through leaks otherwise created in the seals or other structural interfaces of the containers. The vapor loss is typically offset by air ingress into the chambers. Vapor loss and/or air ingress is particularly problematic for dispensers containing medicaments, such as pharmaceutical preparations or vaccines, because they tend to dilute each predetermined dosage of the medicament dispensed from the container, and/or cause the dispenser to dispense inconsistent concentrations of medicament from one dose to the next.

Yet another disadvantage associated with prior art dispensers is that because they cannot reliably maintain the medicament or other substance contained therein in an airtight condition, they cannot be used for either multiple dose applications or preservative-free formulations. The use of single dose dispensers can be substantially more expensive than multiple dose dispensers. In addition, the preservatives used in many medicaments, such as pharmaceutical preparations and vaccines, can cause adverse reactions in patients and/or dilute the effect of the medicament on the patient.

Another drawback of prior art dispensers is that the ullage or "dead space" inherent in such dispensers allows sediment build-up. Many medicaments and other formulations contained within such dispensers are suspensions. The ullage or dead space in the prior art dispensers allows the solutes or other solid components of such suspensions to form sediment therein. Such settling of the suspensions dilutes the medicaments or other substances contained within the dispensers and, in turn, alters the medicament and/or the concentration of medicament in each patient dose.

Another drawback associated with many prior art dispensers is that they can only dispense the medicament or other substance contained therein in an upright or other single orientation. This drawback prevents such dispensers from being used effectively in other orientations, such as upside down. In addition, because such dispensers do not maintain the medicament or other substance contained therein in an airless condition, they cannot be used in low gravity environments, such as outer space.

Accordingly, it is an object of the present invention to overcome one or more of the above-described drawbacks and disadvantages of the prior art.

SUMMARY OF THE INVENTION

In accordance with a first aspect, the present invention is directed to a method for storing and dispensing a sterile fluid. The method comprises the step of storing a sterile fluid in a variable-volume storage chamber of a device hermetically sealed with respect to ambient atmosphere. The device includes a housing, a flexible bladder received within the housing and defining the variable-volume storage chamber, and a one-way valve including an elastic valve member forming a normally closed valve opening. The method further comprises the step of dispensing a plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve by pressurizing fluid at an inlet to the normally closed valve opening and, in turn, moving the valve member between the normally closed position, and an open position. In the open position, at least a segment of the valve member is spaced away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber to allow the passage of fluid from the variable-volume storage chamber through the valve opening. The method further comprises the step of maintaining the sterile fluid within the variable-volume storage chamber sterile and hermetically sealed with respect to ambient atmosphere throughout steps the aforementioned steps.

In some embodiments, the dispensing step includes pumping with a manually-engageable pump, a plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve. In some embodiments, the method further comprises the steps of sterilizing the empty variable-volume storage chamber, and sterile filling the variable-volume storage chamber with the sterile fluid. In some embodiments the dispensing step includes pumping a plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve.

In another aspect, the invention is directed to a device for storing and dispensing a sterile fluid. The device comprises a relatively rigid outer body, a flexible inner bladder received within the outer body and defining a variable-volume storage chamber, and a one-way valve including an elastic valve member forming a normally closed, axially-extending valve opening. The valve member is movable between a normally closed position, and an open position. In the open position, at least a segment of the elastic valve member is spaced away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber to thereby allow the passage of a sterile fluid from the variable-volume storage chamber through the valve opening. The variable-volume storage chamber is filled with the sterile fluid and the sterile fluid is hermetically sealed in the variable-volume storage chamber. The flexible bladder and one-way valve maintain the sterile fluid within the variable-volume storage chamber sterile and hermetically sealed with respect to the ambient atmosphere throughout dispensing a plurality of different portions of the sterile fluid from the storage chamber and through the one-way valve. In some embodiments, the device further comprises a pump for pumping a plurality of different portions of the sterile fluid from the variable-volume storage chamber through the one-way valve.

In another aspect, the invention is directed to a device for storing sterile fluid and dispensing multiple portions of the stored fluid therefrom. The device comprises an outer body and a flexible bladder received within the outer body and defining a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere. The device further includes a one-way valve comprising a valve member formed of an elastic material and forming a normally closed valve opening and an inlet to the valve opening in fluid communication with the variable-volume storage chamber. The valve member is movable radially in response to fluid at the inlet to the valve opening exceeding a valve opening pressure between a normally closed position and an open position. In the open position, at least a segment of the valve member is spaced radially away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber to thereby allow fluid from the variable-volume storage chamber to be dispensed through the valve opening. During dispensing of fluid through the one-way valve, the one-way valve and storage chamber maintain fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere. The device further includes a pump coupled between the variable-volume storage chamber and one-way valve. The pump is configured to pump sterile fluid from the storage chamber and into the valve opening to dispense the fluid therethrough.

In some embodiments, the one-way valve further includes a valve body defining an axially-extending valve seat and a flow aperture extending through at least one of the valve body and the valve seat. The elastic valve member includes an axially-extending valve portion overlying the valve seat and covering a substantial axially-extending portion thereof. The valve portion forms an interference fit with the valve seat. Furthermore, the valve portion and the valve seat define an axially-extending seam therebetween forming the valve opening, and the valve portion engages the valve seat in the closed position. In some embodiments, the valve portion includes a substantially annular segment that engages the valve seat substantially throughout any period of dispensing fluid through the valve opening to maintain a hermetic seal between the valve opening and ambient atmosphere.

In another aspect, the invention is directed to a method for storing sterile fluid and dispensing multiple portions of the stored sterile fluid therefrom. The method comprises the step of storing a sterile fluid in the variable-volume storage chamber of a device hermetically sealed with respect to ambient atmosphere. The device includes a housing, a flexible bladder received within the housing, which defines a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere. The device further includes a one-way valve comprising a valve member formed of an elastic material and forming a normally closed, axially-extending valve opening and an inlet to the valve opening in fluid communication with the variable-volume storage chamber. The method further comprises the step of pressurizing fluid at the inlet to the valve opening to a pressure at least equal to a valve opening pressure and moving the elastic valve member between a normally closed position and an open position. In the open position, at least a segment of the valve member is spaced radially away from the closed position, connecting the valve opening in fluid communication with the variable-volume storage chamber and, in turn, dispensing sterile fluid from the variable-volume storage chamber through the valve opening. During dispensing of fluid through the one-way valve, the method comprises the step of maintaining fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere.

In another aspect, the invention is directed to a device for storing sterile fluid and dispensing multiple portions of the stored fluid therefrom. The device comprises an outer body, and a flexible bladder received within the outer body and defining a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere. The device further comprises means for forming a normally closed opening and an inlet to the opening in fluid communication with the variable-volume storage chamber, for moving, in response to fluid at the inlet to the opening exceeding an opening pressure, between a normally closed position and an open position. In the open position, at least a segment of said means is spaced radially away from the closed position to connect the opening in fluid communication with the variable-volume storage chamber allowing fluid from the variable-volume storage chamber to be dispensed through the opening, and for maintaining fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere during dispensing of fluid through said means. The device further comprises a pump coupled between the variable-volume storage chamber and said means. The pump is configured to pump fluid from the storage chamber and into the opening to dispense the fluid therethrough.

In some embodiments, said means is a one-way valve comprising a valve member formed of an elastic material and forming a normally closed valve opening and an inlet to the valve opening in fluid communication with the variable-volume storage chamber. The valve member is movable radially in response to fluid at the inlet to the valve opening exceeding a valve opening pressure between the normally closed position and the open position. In the open position, at least a segment of the valve member is spaced radially away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber and allow fluid from the variable-volume storage chamber to be dispensed through the valve opening.

In another aspect, the invention is directed to a dispenser for dispensing a fluid. The dispenser comprises a rigid housing, and a flexible bladder mounted within the housing and defining an interior chamber within the flexible bladder, and a fluid-receiving chamber between the flexible bladder and the rigid housing. The dispenser further comprises means for creating a first pressure within the fluid-receiving chamber greater than a second pressure within the interior chamber of the bladder to thereby prevent the ingress of gases or vapors into the fluid-receiving chamber. In some embodiments, the means for creating the pressure differential is formed by a resilient material of the bladder that flexes the bladder outwardly toward an expanded condition, and thereby creates the first pressure within the fluid-receiving chamber greater than the second pressure in the interior chamber of the bladder. Preferably, the resilient bladder is molded in the expanded condition, and therefore the resilient bladder will inherently tend to force itself into the expanded condition and thereby create the desired pressure differential between the fluid-receiving chamber and the interior chamber of the bladder.

In some embodiments, the dispenser further comprises a pump coupled in fluid communication with the fluid-receiving chamber for pumping a fluid received therein from the dispenser; and a one-way valve coupled in fluid communication with the pump for allowing the passage of the pumped fluid therethrough and preventing the passage of fluids in the opposite direction. The one-way valve is preferably formed by a nozzle, and a flexible cover overlying the nozzle and creating the one-way valve at the interface of the nozzle and cover.

In some embodiments, the dispenser further comprises a seal formed between the flexible bladder and the rigid vial for sealing the fluid-receiving chamber. The seal includes a first protuberance extending radially outwardly on an outer surface of the flexible bladder, and a second protuberance axially spaced relative to the first protuberance and extending radially inwardly on an inner surface of the bladder. The first and second protuberances are subject to radial compression to seal the interface between the flexible bladder and rigid vial. In some embodiments, the first protuberance extends about an outer peripheral surface of the bladder and defines an outer annular sealing surface, and the second protuberance extends about an inner peripheral surface of the bladder and defines an inner annular sealing surface. In addition, the first protuberance defines a tapered surface for directing bladder material in approximately the direction of the second protuberance to thereby facilitate maintaining a fluid-tight seal in the event of bladder material creep. The seal further includes a peripheral flange extending about an open end of the flexible bladder and subject to axial compression for further sealing the interface between the bladder and rigid vial.

In some embodiments, the dispenser further comprises a plug receivable within an open end of the rigid vial and engageable with at least one of the first and second protuberances for radially compressing the protuberances to seal the interface between the flexible bladder and rigid vial. The plug defines at least one aperture therethrough in fluid communication with the interior chamber of the flexible bladder. A two-way valve of the dispenser is coupled in fluid communication between the interior chamber of the flexible bladder and the aperture of the plug for preventing fluid communication between the interior chamber of the bladder and the ambient atmosphere when a pressure differential across the two-way valve is less than a threshold level. The two-way valve preferably is formed by a flexible, annular protuberance extending radially inwardly from an inner peripheral surface of the flexible bladder, and engageable with an annular surface of the plug to thereby seal the interface between the flexible bladder and plug. In some embodiments, the annular protuberance defines axially-opposed surfaces that taper inwardly in the radial direction to facilitate flexing of the protuberance in response to the pressure differential across the protuberance exceeding the predetermined threshold level.

The flexible bladder of the dispenser further defines an open end and a closed end, and is movable between a collapsed condition and an expanded condition. Upon expansion of the flexible bladder from the collapsed condition into the expanded condition, the flexible bladder and rigid vial define an annular gap therebetween. In some embodiments, the annular gap defines an increasing width in the axial direction from the open end toward the closed end of the flexible bladder, to facilitate removal of fluid from the fluid-receiving chamber upon expansion of the bladder. Preferably, the flexible bladder initially contacts the rigid vial adjacent to or near the open end of the bladder, and then progressively engages the rigid vial in the axial direction from the open end toward the closed end of the flexible bladder with further expansion thereof. Also in accordance with an embodiment of the dispenser, the flexible bladder defines an external morphology in an expanded condition, the rigid vial defines an internal morphology, and the external and internal morphologies are substantially the same to thereby allow the flexible bladder to conformably contact the rigid vial and substantially eliminate any dead space in the fluid-receiving chamber therebetween.

In some embodiments, the pump of the dispenser comprises a piston, and a slide for slidably receiving the piston therein. At least one of the piston and the slide is reciprocable relative to the other. In addition, the piston is made of a relatively hard material, the slide is made of a relatively soft material, and the piston causes a compression zone of the slide to flex outwardly upon moving at least one of the piston and the slide relative to the other to thereby effect a fluid-tight seal between the piston and slide. In addition, forming the slide from a relatively flexible material allows the slide to be formed integral with a nozzle, such as by molding the two components in a single part, wherein the integral nozzle and slide may be released from a core pin by injecting pressured air therebetween.

Also, in some embodiments, the dispenser further comprises means for controlling the flexible bladder to collapse into a predetermined collapsed condition. In one embodiment, the means for controlling includes a plurality of legs extending axially inwardly into the interior chamber of the flexible bladder for conformably contacting the flexible bladder upon collapse thereof. In another embodiment, the means for controlling is defined by at least one axially elongated surface discontinuity formed in the flexible bladder.

In some embodiments, the dispenser includes a needle penetrable and laser resealable member that is capable of being penetrated by a needle or like injection member for introducing a predetermined substance into the fluid-receiving chamber. In one such embodiment, the flexible bladder includes a first portion substantially infusible in response to the application of thermal energy thereto and compatible with the substance to be received within the fluid-receiving chamber, and a second portion overlying the first portion and fusible in response to the application of thermal energy thereto. Thus, the second portion enables the formation of a substantially fluid-tight seal between the flexible bladder and fluid-receiving chamber in a region thereof penetrated by the needle or like injection member. In one embodiment, the second portion is formed of either a thermoplastic or an elastomeric material, and the bladder, including the first portion thereof, is formed of vulcanized rubber.

One advantage of the currently preferred embodiments of the dispenser is that the pressure differential between the fluid-receiving chamber and the internal chamber of the bladder and ambient atmosphere substantially prevents the ingress of air or other gases or vapors through the flexible bladder, or otherwise into the fluid-receiving chamber. As a result, the dispensers of the present invention may maintain the medicaments or other substances contained therein in an airless condition throughout substantial periods of storage, shelf life and/or use. Accordingly, the dispensers of the present invention are particularly well suited for dispensing multiple doses of non-preserved medicaments or other substances requiring storage in an airless condition.

Another advantage of the currently preferred embodiments of the dispensers is that the seal formed between the flexible bladder and the rigid vial radially and axially directs the material of the flexible bladder to persistently maintain a fluid-tight seal regardless of any creep of the material during the storage or shelf-life of the dispenser. In addition, the one-way valve employed in the preferred embodiments of the present invention further maintains the fluid-receiving chamber in a hermetically-sealed condition throughout the storage, shelf-life and/or use of the dispenser.

Yet another advantage of the currently preferred embodiments of the dispensers is that because the medicament or other substance is maintained in an airless condition in the fluid-receiving chamber, the dispensers may be used in virtually any orientation, and furthermore, may be used in low gravity environments.

Another advantage of the dispensers of the present invention is that the flexible bladder preferably defines an external morphology substantially matching the internal morphology of the rigid vial. As a result, the flexible bladder may expand and conformably contact the rigid vial throughout the interface between these two parts and, in turn, eliminate any dead space within the fluid-receiving chamber.

Yet another advantage of the currently preferred embodiments of the dispensers is that the two-way valve coupled in fluid communication between the interior chamber of the flexible bladder and the ambient atmosphere prevents any exchange of gases or vapors between the interior chamber of the bladder and ambient atmosphere, provided the pressure differential across the valve is less than a predetermined level. As a result, the two-way valve creates a relatively stable micro-atmosphere within the interior chamber of the flexible bladder, thus insulating the interior chamber from fluctuations in pressure and/or humidity in the ambient atmosphere and thereby further preventing the ingress of gas or vapors into the fluid-receiving chamber.

Other objects and advantages of the present invention and/or the currently preferred embodiments thereof will become apparent in view of the following detailed description and accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a partially broken-away, perspective view of an ocular treatment apparatus having a dispenser mounted therein in accordance with a preferred embodiment of the present disclosure.

FIG. **1**A is a view similar to FIG. **1** absent the dispenser.

FIG. **1**B is a perspective view of the ocular treatment apparatus of FIG. **1**.

FIG. **1**C is an exploded view, in perspective, of the ocular treatment apparatus of FIG. **1**B.

FIG. **1**D is an exploded view, in side elevation, of the ocular treatment apparatus of FIG. **1**B.

FIG. **2** is a side elevational view, partly in section, illustrating in further detail the dispenser of FIG. **1** including the pump assembly, vial and a bladder and wherein the pump assembly is disposed in a closed position.

FIG. **3** is a view similar to that of FIG. **2**, although the dispenser is rotated 90° with respect to its orientation in FIG. **2**, and the pump assembly is disposed in an extended position.

FIG. **4** is a central cross-sectional view taken along a longitudinal axis of a piston of the pump assembly of FIG. **1**.

FIG. **5** is a front elevational view of a tip of a nozzle of the pump assembly of FIG. **1**.

FIG. **6** is a longitudinal cross-sectional view taken along line **6**-**6** of FIG. **5**.

FIG. **7** is a central cross-sectional view taken along a longitudinal axis of a slide or body of the pump assembly of FIGS. **2** and **3** and forming essentially the compression zone.

FIG. **8** is a central cross-sectional view taken along a longitudinal axis of a flexible pump cover of the pump assembly of FIGS. **2** and **3**, and illustrating the manner in which the pump cover extends from the tip of the nozzle to the rigid vial and is configured to allow reciprocal movement of the piston connected to the vial.

FIG. **9** is a central, cross-sectional view taken along a longitudinal axis of the rigid vial of the dispenser of FIGS. **2** and **3**.

FIG. **9**A is an enlarged view of a portion of the vial of FIG. **9** showing a rear mounting portion for receiving the bladder of FIG. **10**.

FIG. **10** is a central, cross-sectional view taken along a longitudinal axis of the bladder of the dispenser of FIGS. **2** and **3** showing in this configuration a three-ribbed structure provided to allow the bladder to collapse into a predetermined collapsed condition.

FIG. **10**A is an enlarged view of a portion of the bladder of FIG. **10**.

FIG. **10**B is a highly enlarged view of a portion of the bladder of FIG. **10**.

FIG. **11** is a cross-sectional view taken along a transverse axis of the bladder of FIG. **10**.

FIG. **12** is a schematical view showing, in cross section, another embodiment of the bladder of the dispenser of FIGS.

2 and 3 disposed within the rigid vial and including elongated discontinuities or elongation buffers disposed in an outer wall of the bladder to facilitate the collapse of the arcs that pass through the chords of the respective arcs.

FIG. 13 is a top plan view of the rear plug employed to close the rear end of the inner bladder by forming a sandwich-type structure between the rigid vial and rear plug to hermetically seal the dispenser of FIGS. 2 and 3.

FIG. 14 is a sectional view of the rear plug taken along line 14-14 of FIG. 13.

FIG. 14A is an enlarged portion of the rear plug of FIG. 14 showing further detail of an annular side wall of the plug.

FIGS. 15A-C are sequential side elevational views, partly in section, showing the reduction in volume of fluid and corresponding expansion of the bladder in the full, half-full and empty conditions of the dispenser of FIG. 1, respectively.

FIGS. 16A-C are sequential side elevational views, partly in section, showing the steps of assembling the bladder to the vial during sterilization and filling of the dispenser of FIGS. 2 and 3.

FIG. 17 is a perspective view of another embodiment of a dispenser of the present disclosure.

FIG. 18 is an end elevational view of the dispenser of FIG. 17.

FIG. 19 is a cross-sectional view of the dispenser of FIGS. 17 and 18 taken along line 19-19 of FIG. 18.

FIG. 20 is a cross-sectional view of the dispenser of FIGS. 17 and 18 taken along line 20-20 of FIG. 18.

FIG. 21 is a perspective view of the rear plug of the dispenser of FIG. 17.

FIG. 22 is cross-sectional view of the rear plug of FIG. 21.

FIG. 23 is a partial, enlarged cross-sectional view of the rear plug of FIG. 21.

FIG. 24 is a partial, cross-sectional view of the axially-extending and radially-projecting legs of the rear plug of FIG. 21 illustrating the flexible bladder conformably engaging the legs in the predetermined collapsed condition.

FIG. 25 is a partial, cross-sectional view of the legs of the rear plug and bladder illustrating the bladder in the expanded condition.

FIG. 26 is a cross-sectional view of the flexible bladder of the dispenser of FIG. 17.

FIG. 27 is a partial, enlarged cross-sectional view of a portion of the flexible bladder of FIG. 26.

FIG. 28 is a front elevational view of the integral nozzle and slide of the dispenser of FIG. 17.

FIG. 29 is a cross-sectional view of the integral nozzle and slide taken along line 29-29 of FIG. 28.

FIG. 30 is a side elevational view of the integral piston and rigid vial of the dispenser of FIG. 17.

FIG. 31 is a partial, cross-sectional view of the integral piston and rigid vial of FIG. 30.

FIG. 32 is a cross-sectional view of the flexible nozzle cover and bellows of the dispenser of FIG. 17.

FIG. 33 is a cross-sectional view of another embodiment of the dispenser of the present invention including a resealable portion on the flexible bladder for inserting a needle or like injection member therethrough to fill the dispenser with a medicament or other substance, and allowing the needle holes to be sealed by application of thermal energy thereto.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In FIG. 1, there is shown an ocular treatment apparatus 8 that may be used in conjunction with a dispenser, shown generally at 10, in accordance with the present disclosure. As seen in FIGS. 1 and 1A, the treatment apparatus 8 comprises a housing 12 that may be generally U-shaped in cross section, and defines an interior cavity 14 and an eye cover 16. A trigger 18 is pivotally connected at one end 20 to the housing 12 via a hinge 22, and includes at the other end an arm portion 24 defining a slot 25. As shown best in FIG. 1A, a pin 26 of a wheel 27 is fixedly secured within the slot 25, and the wheel 27 is rotatably mounted on the interior wall of the housing 12. As best seen in FIG. 1, the trigger 18 is elongated and comprises finger grooves 28 for a comfortable fit with, e.g., a patient's hand. An approximately L-shaped spring arm 30 is fixedly secured at one end to a post 29 projecting inwardly from the interior wall of the housing 12, and the spring arm defines a knee or bent portion 31 (shown in phantom) engaging an interior surface of the trigger 18, and a free end 32 engageable with a rim 34 formed at one end of the dispenser 10. An eyelid depressor 36 is pivotally mounted by a hinge 38 to the end of the housing 12 adjacent to the eye cover 16, and includes a hook 40 fixedly secured to the wheel 27 for pivotally moving the eyelid depressor upon actuating the trigger 18.

In use, the eye cover 16 is placed adjacent to the tissue surrounding the eye with the eyelid depressor 36 engaging the tissue adjacent to the ocular cul-de-sac. Upon squeezing the trigger 18, the eyelid depressor 36 rotates in the direction of the arrow 41, and in turn moves the tissue adjacent to the eye to expose the ocular cul-de-sac. Rotation of the eyelid depressor 36 is caused by the wheel 27 which also uncovers a nozzle 42 formed at the adjacent end of the dispenser 10. Simultaneously, the spring arm 30 forces the rim 34 of the dispenser 10 away from the fixed nozzle 42 to thereby prime the pump of the dispenser, as described in further detail below. Upon squeezing the trigger 18 and correspondingly extending the dispenser 10 within the housing 12, the free end 32 of the spring arm 30 eventually disengages itself from the rim 34 of the dispenser to thereby release the extended dispenser from the spring arm. As a result, due to the resiliency or spring-like nature of the nozzle 42, as described further below, the extended dispenser contracts or moves back toward the nozzle and, in turn, releases a predetermined dosage of medicament (or other substance) from the nozzle and into the ocular cul-de-sac of the user's eye. Then, when the user removes the ocular treatment apparatus 8 from his or her eye and releases the trigger 18, the spring arm 30 automatically returns to its original or resting position as shown in FIG. 1 with the free end 32 engaging the rim 34. The force exerted by the spring arm 30 upon returning to its original position also rotatably drives the wheel 27 in the direction opposite that of the arrow 41 and, in turn, causes the eyelid depressor 36 to return to its original position, as shown. The ocular treatment apparatus is then ready to dispense another predetermined dosage of medicament or other liquid contained therein.

Other examples of ocular treatment apparatus that may employ the dispenser 10 are described in U.S. Pat. Nos. 4,981,479 and 6,033,384, which are assigned to the assignee of the present invention and are hereby incorporated by reference as part of the present disclosure. Accordingly, as may be recognized by those of ordinary skill in the pertinent art based on the teachings herein, the dispensers of the present invention may be utilized in any of numerous different apparatus or systems to facilitate holding and dispensing medicaments or other fluids, liquids or other substances contained therein, such as nasal inhalers.

Referring now to FIGS. 2 and 3, the dispenser 10 is shown partly in cross section to illustrate the internal components thereof. The dispenser 10 is generally cylindrical in outer configuration and comprises a pump assembly 50, a generally rigid vial **52**, and a flexible bladder **54** disposed within a main fluid chamber **55** of the vial. The pump assembly **50** comprises a piston **56** for discharging predetermined doses of medicaments or other substances contained within the fluid chamber **55**, a slide or body **60** for slidably receiving therein the piston and defining a predetermined dosage chamber therebetween, and a pump cover **62** forming with a nozzle **58** a one-way valve at the dispensing tip and a spring-like bellows for allowing either the piston or nozzle to be moved toward the other to eject a dose of medicament or other substance through the nozzle, and to force either the piston or the nozzle away from the other upon releasing the predetermined dose. The nozzle **58** hermetically seals the dispensing tip of the dispenser and ejects the pumped medicament or other substance therethrough.

Referring now also to FIG. **4**, the piston **56** may be composed of any durable and moldable material, such as a plastic substance and, preferably, the material is suitable for use in connection with medicaments. A suitable material is a low density polyethylene. The piston **56** comprises a base portion **64**, an elongated portion **66** extending from the base portion **64**, and a central bore **68** which is in fluid communication with the main fluid chamber **55**. The base portion **64** is generally disc-like in outer configuration, and comprises a connecting flange **70**, an annular mounting portion **72**, a first annular groove **74**, and a second annular groove **76** spaced inwardly relative to the first annular groove and surrounding the inlet end of the central bore **68**. The connecting flange **70** is configured to engage, e.g., in a snap-lock manner, the vial **52** defining a correspondingly dimensioned mounting flange **78** (FIG. **2**). As shown in FIG. **2**, the mounting portion **72** and first annular groove **74** receive an annular flange **80** and rib **82**, respectively, of the pump cover **62** which is composed of a flexible material, as discussed in more detail below, and which thereby seals the main fluid chamber **55** of vial **52**. As further shown in FIG. **2**, when the piston **56** is assembled to the vial **52**, the second annular groove **76** is located adjacent to the main fluid chamber **55**. The second annular groove **76** thereby functions to provide a capture area to receive any gas bubbles improperly disposed within the main fluid chamber and to prevent the bubbles from passing into the central bore **68**.

As shown best in FIG. **4**, the elongated portion **66** comprises an annular groove **84**, a laterally-extending bore **86**, and a terminal end defining a receptacle portion **88**. The annular groove **84** is configured to receive a seal **90** (FIG. **2**), such as an o-ring, for sealing the piston in contact with the slide **60**. The laterally extending bore **86** is in fluid communication with the central bore **68** and terminates adjacent to an annular interior surface **92** of the slide **60** (FIG. **3**). As shown best in FIG. **4**, the receptacle portion **88** comprises an annular wall **94**, a tapered portion **95** extending between the annular wall **94** and bore **86**, and a piston surface **96** for stopping movement of the nozzle **58** as described in more detail below in connection with FIGS. **5** and **6**. The annular wall **94** defines a generally increasing outer diameter toward the distal end, and slidably engages the annular interior surface **92** of the slide **60** as described in more detail below in connection with FIG. **7**.

As shown in FIG. **3**, the piston **56** further includes two generally symmetrically-located hook portions **97**, and each hook portion **97** defines in combination with an outer surface **101** of the piston **56** a respective slot **99**. As described in more detail below in conjunction with FIG. **7**, the slide **60** is reciprocally disposed within the slots **99** for allowing relative movement of the piston within the slide upon actuation of the pump.

Referring now to FIGS. **5** and **6**, the nozzle **58** may be composed of any suitably durable, moldable, somewhat flexible material (in the configuration wherein the nozzle and body are made of one piece), such as a plastic material, and currently is composed of a material which has been found to be compatible with medicaments, such as those materials sold under the trademarks VELEX and LEXAN, both owned by the General Electric Company of Pittsfield, Mass. The nozzle **58** is preferably molded of one piece and comprises a truncated, conical-shaped body portion **98**, and a disc portion **100** disposed coaxially with the conical-shaped portion and extending radially therefrom. It will be recognized that the conical-shaped portion **98** and disc portion **100** may be molded together or separately. The conical-shaped portion **98** comprises a tapered outer surface **102**, a partial central bore **104**, and an engagement portion **106**. The partial central bore **104** terminates at a lever wall **108** which is dimensioned and configured to allow flexing of the tapered outer surface **102** in the direction of the arrow **110**. The engagement portion **106** is configured to mate with the receptacle portion **88** of the piston **56**, described above in connection with FIG. **4**, and comprises a truncated conical configuration terminating in an engagement surface **112**. As illustrated in FIGS. **2** and **3**, when the piston **56** reaches the end of its stroke upon dispensing a predetermined dose, the engagement surface **112** of the nozzle is received within the guide wall **94** and engages the piston surface **96** to terminate further movement. It will be recognized that a variable stroke volume **113** is defined between the engagement surface **112** of the nozzle **58** and the piston surface **96** of the piston **56**. As illustrated in FIG. **3**, the maximum stroke volume is defined by the maximum extension of the engagement surface **112** from the piston surface **96**.

As shown in FIG. **6**, the disc portion **100** comprises an annular mounting portion **114** for affixably mounting the nozzle **58** to the pump cover **62** and slide **60** (FIGS. **2** and **3**), and also comprises a slot **116** for the passage of fluid or other substances therethrough. The mounting portion **114** comprises an annular thickened portion **118** and a neck portion **120** disposed between a pair of annular grooves **122** and **124**. As shown in FIGS. **2** and **3**, the annular groove **122** is configured to engage a rib **126** of the pump cover **62** (FIG. **8**), and the annular slot **124** is configured to engage a correspondingly configured terminal end portion **128** of the slide **60** (FIG. **7**). As shown in FIG. **6**, the annular groove **124** defines an annular crevice **130**, employed, e.g., for easing assembly of the slide **60** to the nozzle **58**. The slot **116** is disposed adjacent to a flattened portion **132** of the tapered outer surface **102**, and provides fluid communication from the variable stroke volume **113** through the disc portion **100** to the tapered outer surface.

As illustrated in FIG. **7**, the slide **60** defines a tubular body and may be composed of a similar substance to that described above with respect to the nozzle **58** (FIGS. **5** and **6**). As described above and referring also to FIG. **2**, the slide **60** comprises an annular inside surface **92** within which the piston **56** and engagement portion **106** of the nozzle **58** are disposed after assembly of the dispenser **10**. The inside surface **92** defines a bore **134** with a neck portion **136** of reduced diameter disposed between a first transition zone **138** of relatively rapid increase in diameter, and a second transition zone **140** of relatively gradual increase in diameter. Referring now to FIG. **2**, it will be understood that during relative movement of the nozzle **58** and the slide **60** away from the piston **56**, the annular wall **94** of the piston (FIG. **4**) will engage the second transition zone **140** (FIG. **7**) in sealing engagement to thereby force fluid contained within the variable stroke volume **113** into the slot **116** of the nozzle tip.

With reference to FIG. **7** and as described above in connection with FIGS. **5** and **6**, the slide **60** defines a terminal end **128** that includes an annular ridge **142** configured to engage the crevice **130** of the nozzle **58**. As shown in FIG. **3**, the opposite end of the slide **60** defines a flange **144** that is configured to engage the hook portion **97** of the piston **56**.

FIG. **8** depicts a cross-sectional view of the flexible pump cover **62**. The flexible pump cover **62** may be composed of any durable, resilient and flexible material, such as an elastomeric material. Preferably, the pump cover **62** is composed of a thermo-elastic material, such as a styrene-butadiene elastomer sold under the trademark KRATON by GLS of Illinois. Other suitable materials include polyvinylchloride, Santoprene™ and butyl rubber. The pump cover **62** comprises a mounting portion **146**, a bellows portion **148**, and a nozzle cover **150** which cooperates with the slot **116** (FIG. **6**) to provide an elastic valve, as described further below in connection with FIG. **5**. As described above in connection with FIG. **4**, the mounting portion **146** comprises an annular flange **80** that fits within the mounting groove **72** adjacent to the mounting flange **78** of the vial **52** (FIG. **2**). As shown in FIG. **8**, the rib **82** defines in cross section a truncated conical shape corresponding to the configuration of the annular groove **74** of the piston (FIG. **4**). Because of the resilient nature of the material of the pump cover **62**, the annular flange **80** may be slightly oversized in order to provide a resilient fit with the vial **52** and piston **56** and thereby, in combination with the rib **82**, hermetically seal the main fluid chamber **55** (FIG. **2**).

The bellows portion **148** extends between the mounting portion **140** and nozzle cover **150**, and comprises a plurality serpentine or inversely curled portions **152** which function to provide resiliency in a direction generally parallel to a central axis **154** and sufficient spring-like force to either drive the piston or the nozzle away from the other and return the piston to the top of its stroke upon dispensing a predetermined dose of a medicament or other substance contained within the chamber **55**. Referring also to FIGS. **2** and **6**, the nozzle cover **150**, when mounted, is dimensioned and configured to resiliently engage the nozzle **58** and slide **60**, and includes the annular rib **126** extending axially from a disc engagement portion **156**. The disc engagement portion **156** is disposed between a slide engagement portion **158** and a nozzle body engagement portion **160**. Referring also to FIG. **6**, the nozzle body engagement portion **160** is configured to engage the tapered outer surface **102** of the nozzle **58** to thereby form a normally-closed, one-way valve therebetween. As can be seen in FIG. **8**, the cross-sectional thickness of the nozzle engagement portion **160** gradually decreases in the axial direction from the disc engagement portion **156** toward the dispensing tip **161**. The gradually-decreasing cross-sectional thickness of the nozzle engagement portion **160** facilitates the release of the medicament or other substance through the one-way valve formed by the elongated, annular interface between the relatively flexible nozzle engagement portion **160** of the cover and the tapered surface **102** of the nozzle body, while simultaneously preventing air or other gases from passing through the valve in the opposite direction, in accordance with the teachings of the below-mentioned patents incorporated by reference herein.

In operation, as described above in connection with FIGS. **1** and **1**A, movement of the vial **52** in the axial direction causes the piston **56** to move from the position shown in FIG. **2** into the position shown in FIG. **3** (or vice versa), e.g., by actuating the trigger **28** of FIG. **1** or other actuator, which draws fluid into the variable volume fluid chamber **113** from the main fluid chamber **55** via the central bore **68** and laterally-extending bore **86** of the piston. Referring now also to FIGS. **6** and **8**, as the piston **56** moves toward the nozzle **58** (or vice versa), the fluid is injected through the slot **116** (FIG. **6**), along the flattened surface **132**, between the tapered surface **102** and nozzle body engagement portion **160**, and then outwardly of the nozzle tip. Further details of pump assemblies that may be used in the practice of the present invention are described in U.S. Pat. Nos. 5,944,702, 5,875,931 and 5,746,728, which are assigned to the same assignee as the present invention, and are hereby expressly incorporated by reference as part of the present disclosure.

One advantage of the pump configuration of the illustrated embodiment, and as indicated by the arrow indicating the path of fluid flow in FIG. **6**, the pumped fluid follows a fairly straight path extending in a direction parallel to the axis **154** from the variable stroke volume **113**, over the tapered surfaces of the engagement portion **106**, through the slot **116**, and between the one-way valve formed by the interface of the nozzle engagement portion **160** of the cover and the tapered outer surfaces **132** and **102** of the nozzle body. This relatively straight and smooth fluid flow path allows the pumped fluid to flow through the nozzle with relatively little head loss, thus allowing lesser force to dispense the fluid and otherwise facilitating precise control over the type of fluid flow to be emitted at the dispensing tip, such as control over drop size, flow velocity, or spray droplet size, spray pattern, etc.

Yet another advantage of the illustrated pump configuration is that the bellows **148** is sealed relative to the variable-stroke volume **113** to thereby prevent any of the medicament or other substance contained within the chamber **55** from collecting in the space between the bellows and the piston or slide. As can be seen, the o-ring or like seal **90** forms a fluid-tight seal between the piston and the slide, thus preventing any fluid from flowing therethrough and into the bellows. Similarly, fluid-tight seals are formed at the interfaces of the cover **62**, nozzle **58** and slide **60**, including fluid-tight seals at the interfaces of the slide engagement portion **158** of the cover and the slide **60**, and at the interface of the annular rib **126** of the cover and at the annular groove **122** of the nozzle **58**.

Referring now to FIGS. **9** and **9**A, the vial **52** is preferably composed of a suitably rigid and moldable material, such as a rigid polymeric material, e.g., polycarbonate or polyvinylchloride. Preferably, this material is selected to be compatible with a wide variety of medicaments, such as that sold under the trademark Lexan of the General Electric Corporation of Pittsfield, Mass. The vial **52** is tubular in configuration and comprises an outer wall **77** that defines the main fluid chamber **55**, the annular mounting flange **78** discussed above in connection with FIGS. **2** and **4**, and an annular connecting portion **162** formed on an opposite end of the vial relative to the mounting flange **78**. The main fluid chamber **55** is dimensioned such that it is large enough to contain a predetermined quantity of a fluid to be dispensed, such as a medicament, along with the flexible bladder **54** (FIG. **2**) discussed in more detail below. The mounting flange **78** includes an annular ridge **164** for mounting the vial **52** into sealing engagement with the nozzle cover **62** (FIG. **2**) and preventing movement of the cover during use of the dispenser **10**. As seen in FIGS. **2** and **3**, the mounting portion **146** of the cover **62** is sandwiched between the base **64** of the piston **56** and the rigid vial **52** to form a fluid-tight seal.

As shown in FIG. **9**A, the annular connecting portion **162** comprises a tapered end **166** and a peripheral groove **168** spaced inwardly therefrom on an increased diameter portion **170**. An annular ridge **172** is provided for engaging the flexible bladder **54** (FIG. **2**). As described further below, the increased diameter portion **170** and annular ridge **172** function to allow hermetic sealing of the main fluid chamber **55** after assembly of the vial **52**. As also described further below, an annular groove **174** is provided for retention of the vial **52** during filling of the main fluid chamber **55**.

Referring now to FIG. **10**, the flexible bladder **54** may be composed of any suitably flexible material, and preferably defines barrier properties to prevent the passage therethrough of vapor, moisture and gas. For ease of manufacture, the material preferably may be molded and is compatible with a wide variety of medicaments or other substances to be contained within the chamber **55**, and therefore in a preferred embodiment may be formed of a rubber or synthetic rubber. Alternatively, the flexible bladder **54** may be composed of a thermo-elastic material, such as the styrene-butadiene elastomer sold under the trademark KRATON as discussed above in connection with the pump cover **62**. Similarly, materials sold under the trademarks VISKAFLEX owned by the AES Company, ALCRYN or HYTREL owned by the Dupont Company of Wilmington, D.E., and SARLINK owned by the DSM Company may be used instead. These materials are only exemplary, however. As may be recognized by those skilled in the pertinent art based on the teachings herein, the flexible bladder may be made of any of numerous other materials that are currently or later become known for performing the function of the flexible bladder as disclosed herein.

In the currently preferred embodiments, the flexible bladder **54** is made of a resilient material as described above and is molded in the expanded condition. Accordingly, when collapsed in the manner described further below, the resilient bladder tends to force itself outwardly and, in turn, increase the pressure of the medicament or other fluid in the main fluid chamber **55** in comparison to the pressure in the interior of the bladder. A significant advantage of this pressure differential is that it facilitates in preventing the ingress of air, other gases or vapors located within the interior chamber of the bladder through the bladder or otherwise into the main fluid chamber. As a result, the dispensers of the present disclosure are particularly well suited for containing multiple dose, non-preserved medicaments or other substances, and in maintaining such substances in a sterile, airless condition, throughout substantial periods of storage, shelf life and/or use of the dispensers. This advantageous feature also facilitates in preventing any changes in the ambient conditions of the dispenser from affecting the airless condition of the main fluid chamber **55**, and otherwise prevents the ingress of air, other gases or vapors into the main fluid chamber.

The flexible bladder **54** preferably also provides a barrier to the passage of gas, such as air, through the flexible bladder, and thus may be composed of a single layer of material that has a substantially reduced permeability to air. In one embodiment, the bladder **54** is composed of a multi-layered material. For example, as illustrated in FIG. **10**B, a bladder wall **175** may comprise a first flexible layer **177** of an elastomer that is relatively porous to air, and a barrier layer **179**, such as a metallized MYLAR, e.g., an aluminum and polyester composition, sold by the Dupont Corporation of Wilmington, Del., that is relatively impervious to air. The barrier layer **179** may be disposed between a polyethylene upper layer **181** and lower layer **183** to facilitate adhesion of the barrier layer to the bladder wall **175** while maintaining flexibility. Alternatively, the barrier layer **179** may be composed of polyvinylidene chloride sold under the mark SARAN owned by the Dow Chemical Company of Midland, Mich. It will be appreciated that the barrier layer **179** is preferably dimensioned to cover as much of the bladder wall **175** as permitted in order to reduce the passage of air therethrough without interfering with the various functions of the flexible bladder as more fully described below. The barrier layer **179** is also preferably disposed on the interior of the bladder wall **175**. Optionally, the barrier material may be a butyl rubber-based material, such as that used for the manufacture of syringe stoppers, or used in the tire industry. As may be recognized by those skilled in the pertinent art based on the teachings herein, the flexible bladder and barrier materials disclosed herein are only exemplary, and any of numerous other materials that are currently known, or later become known for performing the functions disclosed herein, may be equally employed.

Referring now again to FIG. **10**, the flexible bladder **54** is tubular in configuration and comprises a closed end **176** and an open end **178** that fluidly communicates with a cavity **180**. The bladder **54** defines an external diameter dimensioned to fit within the vial **52** (FIG. **2**) when in the expanded condition as shown in FIG. **10**. As shown in FIGS. **2** and **3**, the outer surface of the bladder **54** preferably defines a shape or morphology substantially the same as that of the interior surface of the rigid vial **52** so that upon expanding the flexible bladder, the flexible bladder conforms to and contacts the rigid vial throughout the interface of these two components to thereby eliminate any ullage or dead space between the components, and force all of the medicament or other substance within the chamber **55** into the variable stroke volume **113** of the pump **50** for dispensing therefrom. In addition, the outer diameter (or width) of the flexible bladder when fully expanded is preferably slightly greater than the inner diameter (or corresponding width) of the rigid vial, so that the expanded bladder may exert a resilient force against the vial to maintain at least a slight pressure differential between the chamber **55** on one side of the bladder and the interior of the bladder and thereby prevent the ingress of air, other gases or vapors through the bladder and into the main fluid chamber, as described above.

As shown in FIGS. **10** and **11**, longitudinally extending stiffeners or rib portions **182** are disposed along the inside surface **184** and function to provide a supporting structure about which the bladder **54** may collapse as will be described in more detail below in conjunction with FIG. **12**. To achieve this, the rib portions **182** extend axially along the interior surface **184** and are approximately equally spaced about the circumference of the interior surface. It will be recognized that other configurations of the rib portions **182** and/or locations at which the rib portions may be employed are contemplated. For example, the rib portions **182** also may extend along the inside surface **183** of the closed end **176** of the flexible bladder **54**.

As illustrated in FIGS. **10** and **10**A, the flexible bladder **54** includes a mounting portion **186** that comprises an annular flange **188** formed at the rear end of the bladder, an outer annular lobe **190** spaced axially inwardly relative to the flange **188**, and an inner annular lobe **192** spaced between the outer annular lobe **190** and the flange **188**. As shown in FIG. **10**A, the annular flange **188** defines on its underside an annular, V-shaped indent **194** for sealing engagement with the annular ridge **172** of the vial **52** (FIG. **9**A). In addition, the annular flange **188** is over-sized so that during initial assembly with the vial **52**, as will be discussed in more detail below, the peripheral surface of the annular flange may engage the corresponding annular groove **168** of the vial **52** (FIG. **9**A).

During storage and/or shelf life of the dispenser **10**, the material of the flexible bladder **54** may flow or move in order to equalize the tensile and compressive forces that it is subject to. Creep, as used herein, refers to a change in property of the material wherein there is a loss in resilience and memory of the material. In particular, after undergoing creep the elastic material may permanently deform and lose at least some of its original elasticity. Accordingly, after assembly and during filling of the dispenser **10**, the cavity **180** of the flexible bladder **54** may be subject to low pressure which causes collapse and elastic deformation thereof which is maintained by the pressure of fluid filled in the main fluid chamber **55** (FIG. **2**). Thereafter, the filled dispenser may be maintained in storage and/or on a store or other shelf for at least two or more months prior to use, during which the material of the bladder may undergo creep causing at least some deformation thereof. To properly manage the movement of the material during creep of the flexible bladder **54**, and as shown best in FIG. **10**A, the bladder is provided with the outer annular sealing lobe **190** and the inner annular sealing lobe **192** spaced axially between the outer sealing lobe and the flange **188** so that, when creep resulting from compression of the elastomeric or rubber-like material occurs, the intra material pressure is balanced in between the two lobes **190**,**192** and a persistent, fluid-tight seal is provided. This mechanical seal can then be maintained due at least in part to the material reservoir formed by the inner lobe **192** in which creeping material in the outer lobe **190** offsets that of the inner lobe.

As shown in FIG. **10**A, the outer annular lobe **190** comprises a first angular portion **198** located on one side of the lobe **192**, and a second angular portion **200** disposed on the opposite side of the lobe. The first angular portion **198** defines a first acute angle "A" with respect to a center axis **202** that may be within the range of approximately 0° to approximately 30°, and more preferably within the range of approximately 0° to approximately 10°. The second angular portion **200** defines a second acute angle "B" relative to the axis **202** that may be within the range of approximately 0° to approximately 15°, and more preferably within the range of approximately 0° to approximately 5°. In order to ensure that during creeping of the material of the flexible bladder **54** the material moves approximately in the directions of the arrow **204** and arrow **205**, the first angle A is larger than the second angle B and the flexible bladder is axially fixed by the inner annular sealing lobe **192** received within the corresponding annular groove **22** of the rear plug (FIG. **14**). As shown in FIGS. **2** and **3**, when the flexible bladder **54** is fully received within the rigid vial **52**, the outer annular lobe **190** is pressed against the smooth interior wall of the vial, the inner annular lobe **192** is received within the corresponding annular groove **22** of the rear plug (FIG. **14**), and the annular flange **188** is sandwiched between the rear plug and the annular ridge **172** of the rigid vial. Thus, the inner annular sealing lobe **192** functions as a material reservoir for the outer annular sealing lobe **190**, and as indicated by the arrows **204** and **205**, the axially-offset lobes cause the material to flow generally from the outer lobe **190** toward the inner lobe **192**, and from both lobes generally toward the annular flange **188**. As a result, the material flow is persistently directed toward the inner sealing lobe **192** and/or annular flange **188** to thereby maintain a fluid-tight seal between the flexible bladder, rigid vial and rear plug, regardless of the degree of creep of the bladder material. As can be seen, the shape and relative position of the outer annular lobe **190** as described above facilitates in directing the forces within the bladder and thus the material in the directions of the arrows **204** and **205** to thereby maintain the fluid-tight seal throughout the storage, shelf-life and usage of the dispenser **10**.

As shown in FIG. **11**, the flexible bladder **54** preferably also comprises at least one surface discontinuity **206** that facilitates and controls the collapse of the bladder from a tubular configuration to a predetermined collapsed configuration to thereby substantially eliminate the volume of the cavity **180** defined by the interior of the bladder. In the illustrated embodiment, the flexible bladder comprises three surface discontinuities **206** located on the interior surface **184** of the bladder and approximately equally spaced relative to each other. As can be seen, the discontinuities **206** are each approximately equally spaced between adjacent elongated ribs **182**. The discontinuities **206** are illustrated in the configuration of a crevice or crack terminating in a generally flat center portion (not numbered) in cross section as shown. As can be seen, the surface discontinuities **206** cause the bladder to collapse or fold onto itself about each elongated rib **182** to thereby form in the collapsed condition three folded sections or legs spaced about 120° relative to each other. As may be recognized by those skilled in the pertinent art based on the teachings herein, and illustrated by the additional embodiments below, any of numerous other structures or configurations may be equally employed to collapse the bladder into a predetermined shape, such as the predetermined collapsed shape formed by discontinuities and elongated ribs described above.

Referring now to FIG. **12**, a cross section of an outer wall **208'** of a flexible bladder **54'** is illustrated in schematic. The flexible bladder **54'** is capable of collapsing in the direction of arrows **210'** from an expanded position, shown in solid lines adjacent to the outer wall **77** of the vial **52** (FIG. **9**) to a collapsed position shown in broken lines. The flexible bladder **54'** is functionally similar to the flexible bladder **54** and thus like elements are labeled with like reference numerals followed by the prime (') symbol. However, it will be recognized that some differences in structure exist between the flexible bladder **54** and the flexible bladder **54'**. For example, discontinuities **206'** are illustrated as being inverted with respect to the discontinuities **206** and generally cover the entire cross-sectional thickness (t') of the wall **208'**. While the discontinuities **206'** are illustrated as generally arcuate in configuration, it will be appreciated that other configurations, such as that of discontinuities **206**, which also perform the function described below may be employed instead. Also, it will be appreciated that the rib portions **182'** define mounting slots **209'** for receiving therein correspondingly-shaped portions (not shown) of the vial **52**.

It will be understood that both the discontinuities **206** and **206'** function to allow for a reduction in length of the portions of the wall **208'** necessary to collapse the flexible bladders **54** and **54'**. While this function is being described in connection with the embodiment of FIG. **12**, this description is equally applicable to the embodiment of FIG. **11**. As shown in FIG. **12**, the wall **208'** comprises a plurality of wall portions **212'** extending between each discontinuity **206'** and adjacent rib portion **182'**, and as shown in solid lines each wall portion **212'** forms an arc when the bladder **54'** is expanded. It will be recognized that during collapsing of the bladder **54'** in the directions of the arrows **210'**, the wall portions **212'** become approximately linear and form a chord as shown in the dashed and dotted lines, and then inversely arcuate as illustrated in the dashed lines. Accordingly, as illustrated, a length L_1 of the discontinuities **206'** shown in solid lines shortens to a length L_2 shown in dotted and dashed lines to thereby allow free movement of the arcs **212'** in the direction of the arrows **210'**. Once the flexible bladder **54'** has collapsed, the bladder may expand and the wall portions **212'** may freely move in a direction opposite that of the arrows **210'**.

As illustrated in FIGS. **13** and **14**, the flexible bladder comprises a rear plug **214** configured to mate with the open end **178** of the flexible bladder **54** (FIG. **2**) and to seal the flexible bladder **54** disposed between the rear plug and the rigid vial **52**. The rear plug **214** may be composed of any suitably strong, moldable and durable material, such as a polymeric material, e.g., polyethylene, and is preferably composed of Lexan™ or a like polycarbonate for its stress-resistant properties. The rear plug **214** comprises an end wall **216** and a side wall **218** that, as seen best in FIG. **14**A, preferably includes a tapered portion **220** defining a gradually increasing diameter in the direction of the rear end of the plug, an annular groove **222** spaced rearwardly of the tapered portion **220**, a stepped portion **224**, a plurality of outwardly-protruding protective tabs **226** (or bumps for ease of manufacturing) angularly spaced relative to each other about the axis of the plug, and an aperture **228** extending through the side wall for allowing fluid communication between the interior chamber **180** of the bladder and the ambient atmosphere. The tapered portion **220**, because of the increasing diameter thereof, provides for ease of assembly of the plug **214** to the flexible bladder **54** (FIG. **2**) and defines an annular space **230** (FIG. **2**) located between the plug and the adjacent surface of the flexible bladder. As described above and shown in FIGS. **2** and **3**, the annular groove **222** is configured to receive the inner annular lobe **192** (FIG. **10**) and the stepped portion **224** sandwiches the annular flange **188** of the flexible bladder **54** against the annular ridge **172** of the rigid vial. As best seen in FIGS. **13** and **14**, the safety sealing tabs **226** project upwardly and outwardly from the stepped portion **224** and are angularly spaced relative to each other about the axis of the plug. The sealing tabs **226** are provided for locking the plug **214** to the vial **52** (FIG. **2**) and are configured to snap-fit within the annular groove **168** of the vial (FIG. **9**) upon being pressed against the annular flange **188** of the bladder to thereby maintain an airtight seal. In addition, because the sealing tabs **226** are tapered outwardly as shown typically in FIG. **14**A, the tabs easily snap into the annular groove **168** of the vial; however, the tabs cannot be moved out of the groove in the opposite direction and thereby form a tamper-proof seal. The aperture **228** provides for fluid communication between the annular space **230**, chamber **180** (FIG. **2**) and ambient atmosphere, and is illustrated as being generally rectangular in configuration. However, it will be understood that other configurations, such as circular or other shapes, may be employed, providing that a sufficient volume of air may pass therethrough to fill the interior chamber **180** of the flexible bladder **54**.

Returning to FIGS. **10** and **10**A, the flexible bladder **54** also preferably comprises a two-way valve **234** axially spaced below the sealing lobes **190** and **192** for controlling the flow of air between the interior chamber **180** of the bladder and ambient atmosphere. The valve **234** comprises an annular operator **235** projecting inwardly from the interior wall of the bladder and having a generally ridge-like configuration in cross section. As shown in FIGS. **2** and **3**, the end portion of the annular operator **235** engages the annular surface **232** formed at the base of the rear plug **214**, and is disposed between the annular space **230** and the interior chamber **180** of the bladder. The flexible bladder **54** further defines a plurality of support protuberances **236** that are axially spaced adjacent to the annular operator **235** and angularly spaced relative to each other about the axis **202**. The end surface of each protuberance **236** is spaced inwardly relative to the end of the annular operator **235** to thereby allow the operator **235** to engage and seal the interface between the operator and rear plug, while simultaneously ensuring sufficient radial spacing between the rear plug and flexible bladder for allowing movement of the operator **235** in either direction. Thus, as can be seen, the operator **235** and annular wall **232** of the rear plug form a two-way valve allowing fluid to flow therethrough when the differential pressure across the valve is sufficient to axially flex the operator. It will be understood that the rigidity of the operator is set to allow fluid to pass therethrough when the pressure differential exceeds a predetermined threshold pressure. Thus, a significant advantage of the valve **234** is that it maintains a relatively stable micro-atmosphere within the inner chamber **180** of the flexible bladder **54** and prevents a regular exchange of air, other gases or vapors between the micro-atmosphere within the bladder and the ambient atmosphere. For example, the valve **234** allows air to be drawn into the chamber **180** upon dispensing the medicament or other substance from the main fluid chamber **55** to thereby allow the bladder to expand and fill the space of the dispensed medicament. However, the valve **234** otherwise prevents air or vapors from flowing freely between the micro-atmosphere and the ambient atmosphere. Thus, the micro-atmosphere within the chamber **180** may define different pressure and/or humidity levels in comparison to the ambient atmosphere. A significant advantage of this feature is that it insulates the micro-atmosphere from fluctuations in the pressure and/or humidity levels of the ambient atmosphere, thereby maintaining relatively stable pressure and humidity levels within the micro-atmosphere and thus preventing the ingress of air or vapors through the bladder wall and into the main fluid chamber.

In FIGS. **15**A-**15**C, the dispenser **10** is illustrated in the full, half-full and empty conditions, respectively. In FIG. **15**A, the main fluid chamber **55** is filled with, e.g., a medicament (not shown) that the pump assembly **50** may pump outwardly of the nozzle **58**. Accordingly, the bladder **54** is illustrated in a collapsed state. In FIG. **15**B, the flexible bladder **54** is shown in an expanded condition whereby the bladder has expanded to displace the volume of medicament dispensed from the main fluid chamber **55**. To achieve this result, air has passed in the direction of arrow **240**, through the valve **234** and into the interior chamber **180** of the flexible bladder. In FIG. **15**C, the dispenser **10** is illustrated in an empty condition. As can be seen, the bladder **54** is fully expanded against wall **77** of the rigid vial and substantially conforms to the morphology of the rigid vial to thereby eliminate any ullage or dead space and force all medicament or other substances therein into the pump **50**.

Referring now to FIGS. **16**A-**16**C, initial assembly of the dispenser **10** for purposes of sterilization, e.g., by irradiation of energy rays, is illustrated in FIG. **16**A. In particular, the rear plug **214** is fitted to the flexible bladder **54**, and the plug and flexible bladder are partially inserted into the vial **52**. Turning now also to FIGS. **9**A and **10**, the flange **188** of the flexible bladder **54**, when in the partially inserted position, is disposed within the annular groove **168** of the vial **52** to thereby form an air-tight, but not a tamper-proof seal between the bladder and vial. In this state, the dispenser **10** may be sterilized and/or transported in a sealed condition prior to filling the dispenser with a medicament or other substance to be contained therein.

The filling of the dispenser **10** is illustrated schematically in FIG. **16**B, wherein the flexible bladder **54** and plug **214** are separated from the vial **52** so that the main fluid chamber **55** may be accessed for filling. As can be seen, the annular flange **188** of the bladder may be pulled rearwardly and removed from the annular groove **168** of the vial to thereby open the vial and access the main fluid chamber **55**. Preferably, this operation is carried out by transporting the sterilized dispensers through a sterile transfer port, and filling the dispensers within a sterile filling machine of the types disclosed in commonly-assigned U.S. Pat. Nos. 5,641,004 and 5,816,772, which are hereby expressly incorporated by reference as part of the present disclosure. During filling, a vacuum may be drawn on the inner chamber **180** of the bladder to collapse the bladder, and the medicament or other substance to be contained therein may be introduced into the main fluid chamber **55**.

As shown in FIG. **16**C, upon filling the main fluid chamber **55** with the medicament or other substance to be contained therein, the flexible bladder and rear plug assembly are moved into the rigid vial such that the flexible flange **188** of the bladder is moved into engagement with the annular ridge **172**, best seen in FIG. **9**A, and the rear plug is pressed inwardly until the sealing tabs **226** are snapped into place within the annular groove **168** of the vial to thereby form the airtight and tamper-proof seal. The dispenser **10** may then be installed within the ocular treatment apparatus **8** described above or other suitable apparatus for dispensing medicaments or other fluids, such as nasal inhalers.

In FIGS. **17** through **20**, another embodiment of the dispenser of the present disclosure is indicated generally by the reference numeral **310**. The dispenser **310** is substantially similar to the dispenser **10** described above, and therefore like reference numerals preceded by the numeral "3", or preceded by the numeral "4" instead of the numeral "1", or preceded by the numeral "5" instead of the numeral "2", respectively, are used to indicate like elements. The primary differences of the dispenser **310** in comparison to the dispenser **10** are that (i) the rigid vial **352** and piston **356** are formed as integral components; (ii) the nozzle **358** and slide **360** are formed as integral components; (iii) the flexible bladder **354** defines a smooth cylindrical configuration without any discontinuities or ribs formed thereon; and (iv) the rear plug **514** includes a plurality of inwardly projecting legs **538** for controlling the collapse of the flexible bladder into a predetermined collapsed shape.

As shown in FIGS. **21**-**23**, the rear plug **514** defines a plurality of inwardly projecting, axially-elongated legs **538** defining a framework within the interior chamber **480** of the flexible bladder **354** for controlling the collapse of the bladder into a predetermined collapsed shape. As shown in FIG. **21**, the currently preferred embodiment includes three legs **538** angularly spaced approximately 120° relative to each other about the axis of the rear plug. Each leg lies in a respective plane intersecting the axis of the rear plug and defines approximately planar side surfaces **540** extending radially between the axis of the plug and the inner wall of the rigid vial. As shown in FIGS. **19** and **20**, the radial edge **542** of each leg is radially spaced inwardly relative to the inner wall of the rigid vial to thereby allow movement of the flexible bladder between the radial edges of the legs and the vial. As also shown in FIGS. **19** and **20**, the legs **538** extend axially into the interior chamber **480** of the flexible bladder a distance sufficient to allow the legs to control the collapse of the bladder into the predetermined collapsed condition. In the illustrated embodiment, each leg **538** extends along at least about one-half the axial extent of the bladder. As shown in FIG. **24**, in the predetermined collapsed condition, the flexible bladder **354** conformably engages the outer surfaces of the legs **538** to thereby allow the main fluid chamber **355** to be filled with a medicament or other substance. Then, as shown in FIG. **25**, upon dispensing all of the medicament or other substance from the main fluid chamber **355**, the resilient nature of the flexible bladder **354** causes the bladder to expand outwardly away from the legs **538**. As shown typically in FIGS. **19** and **20**, when fully expanded, the flexible bladder **354** conformably engages the inner wall of the rigid vial to thereby eliminate any ullage or dead space and allow all of the medicament or other substance contained with the main fluid chamber **355** to be dispensed therefrom.

As described above, the flexible bladder **538** is preferably made of a relatively low permeability elastomer, such as a vulcanized butyl rubber, or other rubbers. Such rubbers have demonstrated proven stability and/or compatibility with a wide variety of medicaments, such as pharmaceutical preparations and vaccines, and other substances, and therefore are currently preferred for such applications. In the currently preferred embodiment, the flexible bladder **354** is molded in its expanded condition, and when collapsed, the resilient nature of the bladder tends to force the bladder outwardly toward its expanded condition. The resilient forces within the bladder apply a pressure against the fluid within the main fluid chamber **355**, and therefore create a higher pressure in the main fluid chamber **355** in comparison to that of the interior chamber **480** of the bladder. As a result, the pressure differential prevents the ingress of air or other gases or vapors through either the flexible bladder or rigid vial, or otherwise into the main fluid chamber. Thus, the material and/or configuration of the bladder are preferably selected to maintain a pressure differential sufficient to prevent the ingress of air or other gases or vapors into the main fluid chamber under a variety of atmospheric conditions. As described above, the preferred rubber materials disclosed herein for constructing the flexible bladder are exemplary, and numerous other materials that are currently, or later become known for performing the function of the flexible bladder may be equally employed.

As shown in FIGS. **26** and **27**, the spaced protuberances **236** described above in connection with the flexible bladder **54** of FIG. **10**A may be eliminated depending upon the material of construction and/or other structural features of the flexible bladder **354**. In addition, the outer annular lobe may take a shape different than that illustrated above in connection with the bladder of FIG. **10**A. As shown in FIG. **27**, the outer annular lobe **490** is defined by an annular raised or thickened portion, and a tapered surface **498** extending radially inwardly between the lobe or annular raised portion **490** and the outer peripheral surface of the flexible bladder **354**. As shown in FIGS. **19** and **20**, the annular raised portion **490** is squeezed against the inner surface of the rigid vial **352** which, in combination with the axially offset, inner annular lobe **492** being fixedly received within the annular groove **522** of the rear end cap (FIG. **23**), cause the material of the flexible bladder to creep and/or otherwise flow in the directions of the arrows **504** and **505** in FIG. **27** to thereby persistently maintain an airtight seal between the flexible bladder, rear plug and rigid vial. Thus, the end seal of the flexible bladder is both radially compressed at the axially offset lobes between the rear plug and rigid vial, and is axially compressed at the flange between the rear plug and rigid vial.

As shown typically in FIG. **22**, the rear plug **514** defines three apertures **528** approximately equally spaced relative to each other about the axis of the plug. In addition, rather than defining the sealing tabs **226** described above in connection with FIG. **14**, the rear plug **514** defines an annular lobe **526** projecting outwardly from the peripheral surface of the rear plug and dimensioned to be snapped into the annular groove **168** of the rigid vial (FIG. **30**). The dispenser **310** may be sterilized, temporarily closed, re-opened, and filled in the same manner as described above in connection with FIGS. **16**A through **16**C.

As shown in FIGS. **28** and **29**, the nozzle **358** and slide **360** are formed integral with each other. One advantage of this construction over the separate nozzle and slide described above in connection with the previous embodiment, is that the integral construction is typically less costly to manufacture and assemble, and furthermore, reduces the number of seals between components and thereby enhances the overall reliability of the dispenser.

As shown in FIGS. **30** and **31**, the piston **356** and rigid vial **352** are also formed integral with each other. As with the integral nozzle and slide described above, one advantage of this construction over the separate piston and slide described above in connection with the previous embodiment, is that the integral construction is typically less costly to manufacture and assemble, and furthermore, reduces the number of seals between components and thereby enhances the overall reliability of the dispenser. In the currently preferred embodiment, the integral nozzle **358** and slide **360** is made of a relatively soft material, and the integral piston **356** and vial **352** is made of a relatively hard material. In the operation of the dispenser **310**, on the downward stroke of the piston **356**, and upon reaching the compression zone **436** of the slide **360**, the relative hardness and geometry of the illustrated piston causes the piston to force the compression zone **436** of the slide outwardly and thereby form a fluid-tight seal between the piston and slide. As illustrated in FIG. **30**, the tip of the guide wall **394** defines a chamfer for facilitating sliding movement of the piston within the slide.

Forming the integral nozzle and slide of a relatively soft and/or flexible material allows the compression zone **436** of the slide to flex outwardly in order to remove the part from a core pin upon molding the part, and thus enables the nozzle and slide to be integrally molded as a single part. Preferably, compressed air is injected between the core pin and interior surface **392** of the slide to facilitate removal of the part from the core pin (not shown).

As shown in FIGS. **19** and **20**, when the flexible bladder **354** is at or near its fully-expanded condition, an annular gap "C" is formed between the bladder and vial. As can be seen, the width of the gap C gradually increases in the axial direction moving from the rear end cap **514** toward the closed end **476** of the bladder. As can be seen, the gap C starts about half-way down the axial extent of the bladder and reaches its maximum width at the curved portion of the bladder between the side wall and end wall **476**. The gap C may be created by forming the approximately cylindrical side wall of the flexible bladder **354** with a sufficient draft to form the gap upon insertion of the bladder into the rigid vial. The purpose of the gradually-increasing gap C is to force all fluid within the main fluid chamber **355** in the direction toward the pump **350** and prevent the formation of any pockets of fluid within the main fluid chamber that cannot be dispensed therefrom.

As shown typically in FIGS. **19** and **20**, other than the slight differences necessary to create the gap C, the flexible bladder **354** defines approximately the same morphology as the interior surfaces of the rigid vial **352**, thus enabling intimate and conforming engagement of the bladder with the rigid vial upon full expansion of the bladder. In addition, the flexible bladder **354** preferably defines in its fully expanded condition an outer diameter (or width) at least equal to or greater than the inner diameter (or width) of the chamber **355** of the rigid vial. These features, in combination with the resilient nature of the flexible bladder, prevent the ingress of gases or vapors into the main fluid chamber **355**, and ensure usage of substantially all fluid contained within the chamber.

As shown in FIG. **32**, the flexible cover **362** defines an annular mounting flange **380** on one end thereof which is received within a corresponding annular groove **374** formed on the integral piston and rigid vial (FIGS. **30** and **31**) to fixedly secure the flexible cover thereto. In addition, the integral piston and rigid vial defines an annular flange **381** adjacent to the annular groove **374** which is received within a corresponding annular groove **382** of the flexible cover (FIG. **32**) to further secure the cover thereto.

Turning to FIG. **33**, another embodiment of the dispenser of the present invention is indicated generally by the reference numeral **610**. The dispenser **610** is substantially the same as the dispenser **310** described above, and therefore like reference numerals preceded by the numeral "6" instead of the numeral "3", the numeral "7" instead of the numeral "4", or the numeral "8" instead of the numeral "5", respectively, are used to indicate like elements. The primary difference of the dispenser **610** in comparison to the dispenser **310** is that the dispenser **610** includes a resealable bladder to allow the bladder to be filled in a sterile filling machine of the type disclosed in co-pending U.S. Pat. No. 6,604,561, granted Aug. 12, 2003, which is assigned to the same Assignee as the present invention, and is hereby expressly incorporated by reference as part of the present disclosure.

As shown in FIG. **33**, the flexible bladder **654** includes on its closed end **776** a resealable portion **844** overlying the closed end **776**. In the illustrated embodiment, the flexible bladder **354** is formed of a first material compatible with the predetermined medicament or other substance to be contained within the main fluid chamber **655**, and defines on its external side a medicament-exposed surface intended to be exposed or otherwise placed in contact with the predetermined medicament or other substance contained within the main fluid chamber. The resealable portion **844** is penetrable by a needle or like filling member for introducing the predetermined medicament or other substance through the flexible bladder and into the main fluid chamber. The penetrable region of the flexible bladder is formed of a vulcanized rubber, and therefore is substantially infusible in response to the application of thermal energy thereto. The penetrable region of the resealable portion **844**, on the other hand, is fusible in response to the application of thermal energy thereto, thus allowing the penetrable region of the resealable portion to be hermetically sealed upon removing the needle or like filling member therefrom. In the illustrated embodiment, the resealable portion **844** is insert molded onto the rubber bladder during which the thermoplastic resealable layer bonds itself to the underlying rubber layer. If necessary, a mechanical fastener of a type known to those skilled in the pertinent art may be used to facilitate attachment of the resealable portion to the end wall of the flexible bladder.

The resealable member **844** is preferably made of a resilient polymeric material, such as a blend of the polymeric material sold by GLS under the registered trademark KRATON® and a low-density polyethylene, such as the polyethylene sold by Dow Chemical Co. under the trademarks ENGAGE™ or EXACT™. An important feature of the resealable member **844** is that it be resealable to form a gas-tight seal after inserting a needle, syringe or like injection member through the resealable member. Preferably, the resealable member can be sealed by heating the area punctured by the needle in a manner known to those skilled in the pertinent art and described in the above-mentioned co-pending patent application. One advantage of the blended polymer described above is that it is known to minimize the degree to which the medicament or other substance can be absorbed into the polymer in comparison to KRATON® itself.

As shown in FIG. **33**, the rear plug **514** defines a filling aperture **846** formed therethrough and overlying the resealable member **844**. As shown in broken lines in FIG. **33**, a double lumen needle or like injection member **848** may be reciprocally moved through the filling aperture **846** to, in turn, pierce both the resealable member **844** and underlying closed end **776** of the flexible bladder. The injection member **848** is coupled in fluid communication with a source (not shown) of medicament or other substance to be contained within the main fluid chamber **655** and is actuated to fill the chamber with the medicament or other substance. Upon filling the chamber, the flexible bladder **654** is collapsed into its predetermined collapsed condition, as shown above, and the needle is withdrawn. If necessary, a vacuum may be drawn on the interior chamber **780** of the flexible bladder during filling to facilitate collapse of the bladder. Upon withdrawing the needle, a laser or other energy source (not shown) transmits a beam of laser radiation onto the penetrated region of the resealable member to seal the needle hole in the manner described in the above-mentioned co-pending patent application and thereby maintain the medicament or other substance contained therein in a sterile, hermetically sealed condition. The filling aperture **846** may be sealed with a cap **850** (shown in broken lines) to maintain the interior chamber **780** of the flexible bladder in a sealed condition.

The laser or other energy source includes a laser or other suitable radiation source optically coupled to a scanning mirror. The laser includes a commercially available CO_2 or YAG laser. The CO_2 laser operates at a wavelength of approximately 10.6 μm. At this wavelength, absorption of the laser energy is governed by the electrical conductivity of the material. Therefore, an insulating material, such as the elastomeric material of the resealable member **844**, absorbs and converts most of the incident energy into thermal energy to cauterize the receiving surface. The YAG laser operates at wavelength of approximately 1.06 μm. At this frequency, absorption is governed by the lattice atoms. Thus, a clear or transparent polymer with little ionization would be permeable to the laser beam. Accordingly, when employing a YAG laser, it is desirable to add a colorant to the elastomeric material of the resealable member in a manner known to those of ordinary skill in the pertinent art in order to enhance its absorption of the laser energy. A significant advantage of the YAG laser is that the superficial layer of the penetrable region of the resealable member, and any germs, bacteria or other contaminants thereon, are transformed into plasma to rapidly and thoroughly sterilize the effected surface. If necessary, a UV-filtration coating may be applied to the surfaces of the enclosure for the apparatus of the invention to prevent the operators from receiving any unnecessary UV exposure.

The present inventor has demonstrated that beam energies in the range of approximately 15 to 30 W are sufficient to effectively cauterize the surface of the elastomeric resealable member. In addition, bio-burden testing has demonstrated that laser energies of approximately 20 W or greater may achieve a 6.0 log reduction. At these energies, the apparatus of the present invention may effectively sterilize the surface within a cycle time of approximately 0.5 seconds. Accordingly, a significant advantage of the laser cauterization apparatus and method of the present invention is that they may involve significantly shorter cycle times than various direct heat methods. Yet another advantage of the laser cauterization of the present invention, is that it involves both a non-contact method and apparatus, and therefore there is no need to be concerned with the cleaning of a contact head or like heating surface.

After filling the dispenser with the medicament or other formulation and withdrawing the needle **848** from the resealable member **844**, the penetrated region of the resealable member defines a needle hole along the path of the withdrawn needle. Upon withdrawing the needle **848**, the vulcanized rubber base of the bladder is sufficiently resilient to close upon itself in the penetrated region and thereby maintain the dispenser in a sealed condition. However, vapors, gases and/or liquid may be allowed over time to pass through the needle hole, and therefore each dispenser is passed through a sealing station to heat seal the resealable portion promptly after withdrawing the needle therefrom. As indicated above, the laser source and scanning mirror are employed to heat seal the penetrated region of the resealable member. Accordingly, the same type of laser source and scanning mirror as described above may be employed in the heat sealing station to perform this function, or alternatively, a different type of laser system may be employed. In a currently preferred embodiment of the present invention, a CO_2 laser of approximately 50 W is employed to seal a region approximately 0.10 inch in diameter in the resealable member.

One advantage of the illustrated dispenser is that the underlying rubber base of the resealable member thermally insulates the heated region from the medicament in the dispenser to thereby maintain the medicament in the dispenser within an appropriate temperature range throughout the cauterization and heat sealing processes and thereby avoid any thermal damage to the medicament.

As may be recognized by those skilled in the pertinent art based on the teachings herein, numerous changes and modifications may be made to the above-described and other embodiments of the present invention, without departing from its scope as defined in the appended claims. Accordingly, this detailed description of preferred embodiments is to be taken in an illustrative, as opposed to a limiting sense.

What is claimed is:

1. A method for storing and dispensing a sterile fluid, comprising the following steps:

(i) storing a sterile fluid in a variable-volume storage chamber of a device hermetically sealed with respect to ambient atmosphere, wherein the device includes a housing, a flexible bladder received within the housing and defining the variable-volume storage chamber, and a one-way valve including an axially-extending valve seat and an elastic valve member having a thickness and forming an axially-extending interface with the valve seat defining an interference fit therewith, the interface having an axial extent greater than the thickness of the valve member and forming a normally closed axially-extending valve opening;

(ii) dispensing a plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve by pumping fluid along a path extending in a direction substantially parallel to an axis of the one-way valve at an inlet to the normally closed valve opening and, in turn, moving the valve member between a normally closed position, and an open position with at least a segment of the valve member spaced away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber and thereby allow the passage of fluid from the variable-volume storage chamber through the valve opening, wherein, substantially throughout any period of dispensing fluid through the valve opening, a segment of the valve member engages the valve seat to maintain a hermetic seal between the valve opening and ambient atmosphere; and

(iii) maintaining the sterile fluid within the variable-volume storage chamber sterile and hermetically sealed with respect to ambient atmosphere throughout steps (i) and (ii).

2. A method as defined in claim **1**, wherein the dispensing step includes pumping with a manually-engageable pump the plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve.

3. A method as defined in claim **1**, further comprising the steps of:

sterilizing the variable-volume storage chambe while empty; and

sterile filling the variable-volume storage chamber with the sterile fluid.

4. A method as defined in claim **1**, wherein the dispensing step includes pumping the plurality of different portions of the sterile fluid at different points in time from the variable-volume storage chamber through the one-way valve.

5. A method as defined in claim **1**, wherein the path is substantially straight.

6. A device for storing and dispensing a sterile fluid, comprising: a relatively rigid outer body, a flexible inner bladder received within the outer body and defining a variable-volume storage chamber, and a one-way valve including an axially-extending valve seat and an elastic valve member having a thickness and forming an axially-extending interface with the valve seat defining an interference fit therewith, the interface having an axial extent greater than the thickness of the valve member and defining a normally closed, axially-extending valve opening, and an inlet to the axially-extending interface defining a fluid flow path in communication with the variable volume storage chamber and extending in a direction substantially parallel to an axis of the one-way valve, wherein the valve member is movable between a normally closed position, and an open position with at least a segment of the elastic valve member spaced away from the closed position to connect the valve opening in fluid communication with a sterile fluid from the variable-volume storage chamber and thereby allow the passage of the sterile fluid through the valve opening, wherein the valve member is configured so that substantially throughout any period of dispensing fluid through the valve opening, a segment of the valve member engages the valve seat to maintain a hermetic seal between the inlet and ambient atmosphere, the variable-volume storage chamber is filled with the sterile fluid, the sterile fluid is hermetically sealed in the variable-volume storage chamber, and the flexible bladder and one-way valve maintain the sterile fluid within the variable-volume storage chamber sterile and hermetically sealed with respect to ambient atmosphere throughout dispensing a plurality of different portions of the sterile fluid from the storage chamber through the one-way valve.

7. A device as defined in claim **6**, further comprising a pump for pumping a plurality of different portions of the sterile fluid from the variable-volume storage chamber through the one-way valve.

8. A device as in claim **6**, wherein the path is substantially straight.

9. A device as in claim **6**, wherein the valve seat is conically-shaped at the valve opening.

10. A device for storing sterile fluid and dispensing multiple portions of the stored fluid therefrom, comprising:

an outer body;

a flexible bladder received within the outer body and defining a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere;

a one-way valve comprising an axially-extending valve seat and a valve member having a thickness and formed of an elastic material and forming an axially-extending interface with the valve seat defining an interference fit therewith, the interface having an axial extent greater than the thickness of the valve member and defining a normally closed valve opening and an inlet to the valve opening defining a fluid flow path in communication with the variable volume storage chamber and extending in a direction substantially parallel to an axis of the one-way valve, wherein the valve member is movable radially in response to sterile fluid at the inlet to the valve opening exceeding a valve opening pressure between (i) a normally closed position and (ii) an open position with at least a segment of the valve member spaced radially away from the closed position to connect the valve opening in fluid communication with the sterile fluid and thereby allow the sterile fluid to be dispensed through the valve opening, wherein the valve member is configured so that substantially throughout any period of dispensing fluid through the valve opening, a segment of the valve member engages the valve seat to maintain a hermetic seal between the inlet and ambient atmosphere, and wherein during dispensing of fluid through the one-way valve, the one-way valve and storage chamber maintain fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere; and

a pump coupled between the variable-volume storage chamber and one-way valve and configured to pump sterile fluid from the storage chamber and into the valve opening to dispense the fluid therethrough.

11. A device as defined in claim **10**, wherein the one-way valve further includes a valve body defining the axially-extending valve seat and a flow aperture extending through at least one of the valve body and the valve seat, the elastic valve member includes an axially-extending valve portion overlying the valve seat and covering a substantial axially-extending portion thereof, the valve portion and the valve seat define an axially-extending seam therebetween forming the valve opening, and the valve portion engages the valve seat in the closed position.

12. A device as defined in claim **11**, wherein the valve portion includes said segment that engages the valve seat substantially throughout any period of dispensing fluid through the valve opening to maintain a hermetic seal between the valve opening and ambient atmosphere, and said segment is substantially annular.

13. A device as defined in claim **10**, wherein the variable-volume storage chamber stores the sterile fluid therein in a substantially airless condition during shelf life and dispensing of sterile fluid through the one-way valve.

14. A device as in claim **10**, wherein the path is substantially straight.

15. A method for storing sterile fluid and dispensing multiple portions of the stored sterile fluid therefrom, comprising the following steps:

storing a sterile fluid in a variable-volume storage chamber of a device hermetically sealed with respect to ambient atmosphere, wherein the device includes a housing, a flexible bladder received within the housing and defining a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere, and a one-way valve comprising an axially-extending valve seat and a valve member having a thickness and formed of an elastic material and forming an axially-extending interface with the valve seat defining an interference fit therewith, the interface having an axial extent greater than the thickness of the valve member and forming a normally closed, axially-extending valve opening and an inlet to the valve opening;

pumping sterile fluid along a path extending in a direction substantially parallel to an axis of the one-way valve at the inlet to the valve opening to a pressure at least equal to a valve opening pressure and, in turn, moving the elastic valve member between (i) a normally closed position and (ii) an open position with at least a segment of the valve member spaced radially away from the closed position and, in turn, dispensing sterile fluid from the variable-volume storage chamber through the valve opening, wherein substantially throughout any period of dispensing fluid through the valve opening, a segment of the valve member engages the valve seat to maintain a hermetic seal between the inlet and ambient atmosphere; and

during dispensing of fluid through the one-way valve, maintaining fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere.

16. A method as defined in claim **15**, further comprising the step of pumping fluid from the storage chamber and into the valve opening to dispense the fluid therethrough.

17. A method as defined in claim **15**, wherein the path is substantially straight.

18. A device for storing sterile fluid and dispensing multiple portions of the stored fluid therefrom, comprising:

an outer body;

a flexible bladder received within the outer body and defining a hermetically sealed, variable-volume storage chamber containing therein multiple portions of sterile fluid hermetically sealed with respect to ambient atmosphere;

means for forming an axially-extending interface with a valve seat defining an interference fit therewith and a normally closed opening and an inlet to the opening defining a fluid flow path in communication with the variable volume storage chamber and extending in a direction substantially parallel to an axis of the axially-extending interface, the means also for moving in response to fluid at the inlet to the opening exceeding an opening pressure between (i) a normally closed position and (ii) an open position with at least a segment of said means spaced radially away from the closed position to thereby allow sterile fluid from the variable-volume storage chamber to be dispensed through the opening, for forming a segment that engages the valve seat substantially throughout any period of dispensing fluid through the valve opening to maintain a hermetic seal between the inlet and ambient atmosphere, and for maintaining fluid remaining in the storage chamber sterile and sealed with respect to ambient atmosphere during dispensing of fluid through said means, wherein said means defines a thickness, and the axially-extending interface defines an axial extent greater than the thickness; and

a pump coupled between the variable-volume storage chamber and said means and configured to pump fluid from the storage chamber and into the opening to dispense the fluid therethrough.

19. A device as defined in claim **18**, wherein said means is a one-way valve comprising a valve member formed of an elastic material and forming a normally closed valve opening and an inlet to the valve opening in fluid communication with the variable-volume storage chamber, wherein the valve member is movable radially in response to fluid at the inlet to the valve opening exceeding a valve opening pressure between (i) the normally closed position and (ii) the open position with at least a segment of the valve member spaced radially away from the closed position to connect the valve opening in fluid communication with the variable-volume storage chamber and thereby allow fluid from the variable-volume storage chamber to be dispensed through the valve opening.

20. A device as in claim **18**, wherein the path is substantially straight.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 8,240,521 B2
APPLICATION NO. : 11/351716
DATED : August 14, 2012
INVENTOR(S) : Daniel Py and Joseph M. Ting

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page:

Item (75) Inventors: After "Daniel Py, Larchmont, NY" add "Joseph M. Ting, Fairfield, CT"

In the claims:

Claim 3, column 27, line 6, "storage chambe" should be changed to --storage chamber--

Signed and Sealed this
Second Day of October, 2012

David J. Kappos

David J. Kappos
Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 8,240,521 B2
APPLICATION NO. : 11/351716
DATED : August 14, 2012
INVENTOR(S) : Daniel Py

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title Page:

The first or sole Notice should read --

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 529 days.

Signed and Sealed this
Twenty-third Day of July, 2013

Teresa Stanek Rea
Acting Director of the United States Patent and Trademark Office